PRINCIPLES OF DEFINITION IN MEDICINE

WITH SPECIAL REFERENCE TO CHRONIC BRONCHITIS AND EMPHYSEMA*

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IN the search for a workable definition of "a disease", the dictionaries do not help at all; for their definitions are mostly tautologous. Two dictionaries which I have consulted define it as "a condition of the body or of some part or organ of the body in which its functions are disturbed or deranged"; and as "a definite morbid process having a characteristic train of symptoms". These definitions, equating the definiendum with such abstractions as "a condition" or "a process", are of no practical use. The only useful basis for a definition in a scientific field must be observable phenomena—in this instance the phenomena observed in organisms whose functions or structure are deranged. I suggest the following as a general definition of "a disease":

The term "a disease" refers to those abnormal phenomena which are common to a group of living organisms with disturbed structure or function, the group being defined in a stated way.

Definition of Individual Diseases

The concept of a disease is thus an abstraction from the reality of phenomena observed in patients, useful because it permits of thinking, speaking, and writing in generalisations. The translation of this abstraction into terms of observable phenomena depends upon the sort of criteria used in the definition of the individual disease; or, to put the matter in another way, the meaning of the sentence "this patient is suffering from *x*", where *x* is the name of a disease, depends upon the way in which the group from which the concept of *x* is an abstraction has been defined. It may in fact have been defined in one of several fundamentally different ways. If it has been defined ætiologically—i.e., in terms of specific causative factors—the sentence proclaims that we know (or think we know) the cause of the illness. If the group has been defined in terms of morbid anatomy, the sentence states our belief that certain morbid anatomical changes are present. If, as is often the case, *x* can be defined only on a descriptive basis—i.e., as a syndrome—the sentence simply states that the patient's illness conforms to a certain description.

It is unfortunate that the grammatical form of sentences in which the names of diseases appear suggests that these names refer to agents which are causing the phenomena observed in the patient. If the disease has been defined ætiologically, or if its ætiology is known, there is of course some spurious plausibility in the naive idea that the "disease" is something which attacks the patient and has an independent existence, since it is easy, in translating a sentence containing the name of the disease into factual terms, to fall into the error of identifying the disease with its cause. If a patient has typhoid fever, he may with reason be thought to have been "attacked" by the typhoid bacillus, even though it is clearly erroneous to equate "typhoid fever" with "the typhoid bacillus". The factual analysis of sentences which include the names of diseases defined other than ætiologically is, of course, very far removed from anything that would be implied by this naive interpretation.

The danger of being misled into thinking in this way often arises, sometimes in subtle ways. It may be illustrated rather crudely by the following incident:

I was once discussing the case of a patient with respiratory symptoms with some postgraduate students and had shown them a bronchogram which, we agreed, showed some bronchial dilatation. I asked one of them the cause of the bronchial dilatation, and received the triumphant reply, "Bronchiectasis!". Rather cruelly, I asked him if he regarded bronchiectasis as a little demon who goes about dilating people's bronchi.

The matter is further complicated by the fact that, as knowledge increases, the definitions of diseases tend to evolve from an initial clinical-descriptive, through a pathological, to an ætiological basis. I intend "pathological" to include both anatomical and physiological aspects—i.e., definition by specified disturbances of structure or of function. This may be exemplified well by the evolution of the concept of tuberculosis. At first the various manifestations of disease which we now group together under this heading could be defined only descriptively, and were given such names as "pulmonary consumption", "scrofula", "Pott's disease", and "tabes mesenterica"; then the discovery that a single primitive lesion, the tubercle, was common to them led to their being grouped together under the morbid anatomical term "tuberculosis"; and finally, with the discovery of the tubercle bacillus, it became possible, and more useful, to define this term, by origin morbid anatomical, on an ætiological basis.

When the current state of knowledge permits more than one possible basis of definition of a disease, an ætiological basis will usually be more useful than a pathological, and a pathological than a syndromal. Whatever basis of definition is selected from those possible as most useful, the defining characteristics should be as few as possible, and should be capable of being stated clearly and unequivocally. Unless the disease being defined is a subgroup of a larger group already defined, defining characteristics should be all of the same general type—i.e., all ætiological, all morbid-anatomical or physiological, or all clinical.

Definition and Description

Definition is a statement of the criteria by which in principle (though not always in practice) it can be determined with certainty whether any given example falls into the category to which a name is to be applied. It may be convenient to choose defining characteristics which cannot be directly observed or determined in every case, circumstantial evidence being relied upon in some cases. This is often so even in groups which are defined ætiologically; for example, although the most satisfactory definition of influenza is "the disease caused by the influenza virus" we may quite legitimately make this diagnosis without actually isolating the virus, relying upon indirect evidence from serological tests, or even, during an epidemic, upon clinical evidence only.

* An opening contribution to a guest symposium on the Definition and Classification of Pulmonary Emphysema held at the Ciba Foundation in September, 1958.

A summarised description is often put forward to do duty as a definition, but description must be distinguished clearly from definition. Although in practice knowledge does not grow in this orderly fashion, in principle the correct procedure should be to choose the most useful essential defining characteristics, and then to ascertain by appropriate studies the other characteristics of the group so defined. Upon the total picture thus revealed, the description of the disease should be based. Features of inconstant occurrence have no place in a definition, though they must be mentioned in a description, which should indeed include an estimate of their frequency.

If we adopt a clinical or syndromal definition, we must be prepared to find inconstant morbid anatomy and physiology, and possibly various ætiological factors; and these we shall include in our description of the group. If we adopt a physiological definition we shall have, a priori, unifying features in the physiology, but we must be prepared for greater variability in clinical, anatomical, and ætiological features; and so on. Sometimes a group defined by one type of criterion will be found to have distinctive characteristics of another type; we shall no doubt be pleased by this, for it will simplify our problems, but we have no right to expect it. More frequently it will be found that characteristics of types other than that to which the defining characteristics belong are only partially discriminatory, and often they may not discriminate at all between the defined and some other diseases.

Where there are apparently alternative defining characteristics for a disease, it will usually be found that the groups defined by the two sets of characteristics are not in fact identical. For example, consider " myxœdema " defined descriptively, and " hypothyroidism ", defined in terms of a specific disorder of function. A high proportion of cases in each group will belong also to the other, and for these the two terms might be considered truly alternative. But the group " myxœdema " will include some cases showing a localised change of the defined type, but with evidence of hyperthyroidism; while the group " hypothyroidism " will contain a considerable number of cases without myxœdema.

Diagnostic Criteria

We must also distinguish clearly between defining characteristics and diagnostic criteria. As I have already said, the defining characteristics are those by which in principle, and given opportunities of study of the type to which they belong, it can be established beyond doubt that a case falls into the defined group.

Diagnostic criteria are the considerations upon which a probable diagnosis may be based in practice, and may include characteristics ascertained by any method of study. Only for a disease which is defined on a clinical or syndromal basis will the defining characteristics be an obligatory part of the clinical diagnostic criteria, though even here they will not always be the whole of the possible diagnostic criteria. For diseases defined on other bases, especially morbid-anatomical, clinical diagnostic criteria will often be derived in large part from data obtained from methods of study other than that upon which the definition is based. These, as already noted, may give results only partially discriminatory from other diseases, so that their diagnostic significance can be expressed only as a probability.

To illustrate this by an imaginary example, let us consider a disease x which has been defined on a morbid anatomical basis, but in which the site of the characteristic changes is not accessible to biopsy. That a case falls into this group cannot be established with certainty except by necropsy. The process of clinical diagnosis may be something like this. The clinical picture (history and physical signs) is compatible with x, but might be produced also by several other diseases. Radiological studies give results compatible with, say, three of these possible diseases. Physiological studies give results which are known to occur in 80% of cases of x, never in one of the other diseases, and in 10% of cases of the third. This third disease is known to be rare in the racial group to which the patient belongs, whereas x is fairly common. An empirical test whose theoretical background is poorly understood is known to be positive in 75% of cases of x although 5% of tests give false positive reactions; it is found to be positive in the patient. None of these points is conclusive, and none gives direct information about the defining characteristics; but together they reach a degree of probability fully justifying a diagnosis upon which practical management may be based.

Definition of " Chronic Bronchitis "

In discussions of the groups of patients usually referred to as suffering from " emphysema " and " chronic bronchitis ", the difficulties attendant upon these logical considerations abound. With regard to chronic bronchitis, it is generally agreed that, although the name etymologically should refer to a group defined on a morbid-anatomical basis, such a definition is not possible. The least unsatisfactory definition possible is by clinical description and exclusion:

> Chronic bronchitis refers to the condition of those patients suffering from chronic or recurrent cough and expectoration, in whom these symptoms are not caused by disease of the lungs, by localised disease of the bronchi, trachea, or upper respiratory tract, or by primary cardiovascular disease.

With this definition, to say that a patient suffers from chronic bronchitis is simply a convenient brief way of describing his symptoms. It is potentially misleading to use the term " chronic bronchitis " as if it referred to an agent which could cause emphysema or any other anatomical change; though it is important to investigate the morbid-anatomical changes which may develop in chronic bronchitic patients, and we know that emphysema is one of them.

Basis of Definition of Emphysema

It would be presumptuous of me to offer a complete definition of emphysema; but I should like to make some observations about the basis of such a definition. I think that as the term indicates (and was originally applied to) a morbid-anatomical state, and can be defined in these terms, the primary definition of it should be anatomical. We must accept the possibility that correlation of emphysema so defined with clinical, physiological, and ætiological features may be complex, and that complete certainty in diagnosis during life may not always be feasible. This is a situation with which the clinician is entirely familiar in other contexts. Some physiologists may not have become quite so well reconciled to this lack of certainty, and because of this may wish to suggest a physiological definition of emphysema. This would almost certainly place the morbid anatomists in an even more confused position in the matter of nomenclature than are the physiologists and clinicians at present; for what would morbid anatomists do if—as I suspect they would—they found changes of the type which at present

they call emphysema in patients who had not been found to have the pattern of disturbed function defined by the physiologists as " emphysema "? As far as I can see, an early consequence of a physiological definition of emphysema would be the need to coin at least one new morbid-anatomical term.

The better procedure for the physiologists, in my view, is to define patterns of disturbed function when these are seen to emerge clearly, and then to investigate the correlation of these with morbid anatomy. If a pattern of disturbed function is found to occur only and invariably with a single type of morbid-anatomical change, this could properly be indicated by naming it the functional pattern of that change. But if, as is perhaps more likely, a recognisable pattern of disturbed function is found to be associated with more than one morbid-anatomical pattern, then a name indicative of its physiological basis should be found for it; for in no other way can the ascertained facts be discussed conveniently and intelligibly.

We have an excellent example of this procedure in the closely related field of cardiology, where the various patterns of disturbed function caused by cardiac abnormalities are defined and named primarily in functional terms. This permits clear discussion of the varied relationships of these patterns with equally well-defined morbid-anatomical changes, and also admits the possibility of referring simply to a functional disturbance without implying anything about its morbid-anatomical basis. For example, we can make a diagnosis of congestive heart-failure and then discuss its anatomical basis quite separately.

A general agreement on some terms that could be used to refer to syndromes of disturbed respiratory function, defined on a physiological basis and recognisable with a reasonable degree of probability by methods available to the clinician, would be the most valuable aid to clarity of thought and communication in this field. My present impression is that it would be better to classify (as well as define) emphysema on a morbid-anatomical basis, and the syndromes of disturbed function on a physiological basis, and to investigate the correlations between the two, than to attempt a comprehensive classification including both aspects. The condition of an individual patient would then be described by terms derived from both these classifications.

We also need a convenient term having a broad clinical definition with which to refer to the group of patients commonly described in this country as suffering from " chronic bronchitis and emphysema ". The term " chronic bronchitis ", as I have defined it, is broad enough, but may not be generally acceptable, especially outside this country. It also suffers the etymological disadvantage of suggesting unjustifiably an inflammatory-origin. However, it is well established in usage, and certainly we need either it or a new word with the same definition to refer to the earlier non-disabling phases. For the later stages, perhaps we can do no better at present than " chronic bronchitis with pulmonary insufficiency ".

These terminological matters are of great importance, for our choice of words inevitably influences our subsequent thought. Before coming to any conclusions we should perhaps recall the words of Laennec:

" Rien ne nuit plus aux progrés d'une science que de détourner sans motifs suffisans les noms de leur acception reçue, ou d'en créer de mauvais."

EXUDATIVE ENTEROPATHY

ABNORMAL PERMEABILITY OF THE GASTROINTESTINAL TRACT DEMONSTRABLE WITH LABELLED POLYVINYLPYRROLIDONE

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" HYPERCATABOLIC hypoproteinæmia " is the term used by Schwartz and Thomsen (1957) to describe an alteration in the metabolism of plasma-proteins which results in rather severe hypoproteinæmia. In addition to their report, others have described adult patients (Freeman and Matthews 1958, Pearson et al. 1958) and children (Ulstrom et al. 1956, 1957) with a similar clinical picture, and offer evidence, derived from isotopic turnover studies, indicating that the deficiency of circulating plasma-proteins is related to an excessive rate of destruction, rather than to a failure of protein synthesis. Several older reports are considered by Schwartz and Thomsen (1957) to describe similar cases of idiopathic hypoproteinæmia, although in the majority of these instances the methods available did not permit distinction between failure of synthesis and excessive destruction.

Citrin et al. (1957) investigated thoroughly a patient with giant hypertrophy of the gastric mucosa—a disease often associated with a severe hypoproteinæmia. The results of a study of the turnover of ^{131}I-labelled human serum-albumin in their patient are virtually indistinguishable from the results reported by Schwartz and Thomsen 1957, Freeman and Matthews 1958, and Pearson et al. 1958, except that in the patient with gastric disease it was possible to recover from the lumen of the stomach enough labelled albumin to account for the exaggerated rate of loss from the plasma. Similarly recent investigations at the National Institutes of Health (Steinfeld et al. 1957) have indicated that an analogous process occurs in patients with regional enteritis or chronic non-specific ulcerative colitis. In the latter work, quantitative recovery of labelled albumin from the lumen of the bowel was not feasible although the presence of albumin in the intestine was demonstrated in some of the patients by a qualitative immunochemical procedure. As a substitute, the use of ^{131}I-labelled polyvinylpyrrolidone (P.V.P.) was introduced. This plasma-protein substitute, if it gained access to the gastrointestinal tract after intravenous administration, was excreted with the fæces and could be estimated easily therein.

The purpose of the present report is to describe the test procedure using labelled polyvinylpyrrolidone and to relate in preliminary form the results of the application of this test to patients with " idiopathic hypercatabolic hypoproteinæmia ".

Methods

^{131}I-labelled P.V.P. was produced by a method which has been reported (Gordon 1958) and prepared for intravenous administration by the pharmacy department of the National Institutes of Health Clinical Center. 10–25 μc of radioactivity was injected intravenously in each subject, and a single 96-hour pooled fæcal collection instituted. The great majority of the subjects were given sufficient potassium iodide to prevent thyroidal uptake of any ^{131}iodide that might be liberated, although human and animal studies of thyroidal radioactivity after parenteral injection of ^{131}I-P.V.P. have indicated that without this precaution only traces of radioactivity are accumulated

(R. S. Gordon, unpublished). The fæcal specimens, collected in gallon-size paint cans, were all adjusted to a standard gross weight with water, treated with approximately 20 g. phenol to arrest bacterial fermentation, and homogenised by agitation of the can on a ' Red Devil Paint Conditioner '. The specimens, together with similarly prepared aliquots of the solution of ^{131}I-P.V.P., were assayed in a large well-type multiple-element Geiger counter,* and the fæcal ^{131}I-P.V.P. excretion was expressed as a percentage of the dose administered (corrected, as necessary, for physical decay).

Results

An adverse side-effect of the administration of labelled P.V.P. was encountered in only one subject. This patient, a young woman who might have had previous contact with P.V.P. in cosmetic preparations, complained of itching about the mouth immediately after the injection. There were no visible lesions, and the symptom responded quickly to diphenhydramine.

Fractions of the intravenously administered P.V.P. ranging from zero to 1·5% were found in the fæces of subjects who either had no disease or were in hospital on account of disorders not affecting the gastrointestinal tract or the metabolism of plasma-proteins. The distribution of these results is presented as a histogram in fig. 1. As a means of ascertaining that hypoproteinæmia per se did not influence this result, the test was performed on four subjects with nephrotic syndrome, six with hypoproteinæmia attributable to hepatic disease, three with hypoproteinæmia associated with advanced malignancy, and one with agammaglobulinæmia. In none of these did the fraction of the dose of P.V.P. excreted in the fæces fall outside the normal range.

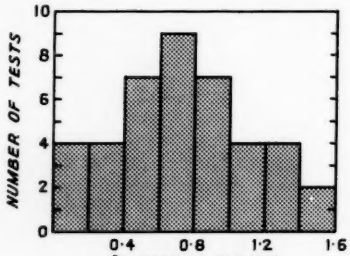

Fig. 1—Fæcal output of intravenously injected ^{131}I-P.V.P. in 41 control studies.

The ^{131}I-P.V.P. excretion test has been applied to nine subjects suffering from " hypercatabolic hypoproteinæmia ", with findings presented graphically in fig. 2. In this figure the percentage of the dose excreted in the fæces is plotted against the patient's serum-albumin level, determined by a modification of the method of Rutstein et al. (1954). If the result of the P.V.P. excretion test is a valid measure of the permeability of the gastrointestinal tract to plasma-albumin, and the hypoalbuminæmia results from loss of protein into the gastrointestinal tract in the presence of an unimpaired rate of albumin synthesis, the anticipated relationship between albumin level and the result of the P.V.P.-excretion test is approximately hyperbolic in form. It may be seen that the results of the study are compatible with this interpretation.

A complete presentation of the clinical features of each of the nine cases of " hypercatabolic hypoproteinæmia " is beyond the scope of this paper, but will be published subsequently (Waldmann and Gordon). Each subject had dependent œdema as his principal complaint and major finding on physical examination. The majority had no complaints referable to the gastrointestinal system; a few had minor symptoms that would ordinarily not have been considered to be significant. X-ray examination of the colon, stomach, and small intestine was performed in each subject. In four no abnormality was noted, whereas in the remaining five there were various minor, non-specific changes which seemed for the most part to be a consequence, rather than the cause, of the hypoproteinæmic œdema. In two subjects a satisfactory study of the rate of degradation of ^{131}I-labelled human serum-albumin had been performed elsewhere; in the remainder this procedure was carried out at the National Institutes of Health by Dr. T. Waldmann and Dr. J. Steinfeld (National Cancer Institute). In all cases there was abnormally rapid degradation of the isotopic albumin. The majority of these patients were young adults, the sexes being approximately equally represented. Two were children; one of these cases, in a boy of two, resembled the cases reported by Ulstrom et al. (1956, 1957) and should, in our opinion, be tentatively classified with them. To date no case with the clinical features of " idiopathic hypercatabolic hypoproteinæmia " has shown a normal ^{131}I-P.V.P.-excretion test.

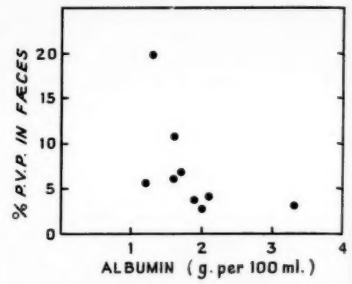

Fig. 2—Relation of serum-albumin level to fæcal ^{131}I-P.V.P. output in 9 cases of exudative enteropathy.

Discussion

These findings implicate the gastrointestinal tract as the route of loss of proteins from the plasma in the disorder known as " hypercatabolic hypoproteinæmia ". Since loss of protein into the stomach or intestine is so similar in its metabolic implications to loss by way of the urine or the skin, it seems appropriate to designate this disorder " exudative enteropathy ", and to reserve the term " hypercatabolic hypoproteinæmia " for cases with true exaggeration of endogenous catabolism.

Exudative enteropathy is a manifestation of disease, and not a true disease entity. Like proteinuria, it will probably be found to occur in several diseases that can be distinguished on the basis of other procedures. The anatomical basis of the disorder in the patients reported here has not yet been elucidated.

Summary

^{131}I-labelled polyvinylpyrrolidone serves as a means for demonstrating an abnormal permeability of the gastrointestinal tract to macromolecules.

This finding is associated with hypoproteinæmia and unimpaired protein synthesis—a disorder for which the term " exudative enteropathy " is suggested.

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* Model WC-3, Nucleonic Corporation of America, Brooklyn, New York.

GASTROINTESTINAL PROTEIN LOSS IN IDIOPATHIC (HYPERCATABOLIC) HYPOPROTEINÆMIA

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THE term "idiopathic" or "essential" hypoproteinæmia bears witness to the ignorance regarding the often greatly reduced serum-protein level in a small but interesting group of patients. Other designations, such as œdema disease, "nephrosis without nephrosis", nephrosis without albuminuria, and hypercatabolic hypoproteinæmia describe certain characteristics of this condition.

The hypoproteinæmia affects particularly the albumin fraction; and the main—often the sole—sign is œdema, which may become extensive and even fatal. The disease appears to be most common in children, who sometimes recover spontaneously. Increased serum-cholesterol, as in nephrosis, is never present. The majority of the 40 reported cases [1–5 7–17 19–30 32–35 38 39 41 42] have been submitted to very thorough investigation of practically all organ systems, but the hypoproteinæmia has not been explained by these studies or by necropsy, which has been carried out in several cases.

In theory hypoproteinæmia may result from: (1) reduced protein synthesis, or (2) enhanced protein loss, which may be external or internal.

Synthesis of protein, particularly the albumin fraction, may be reduced in hepatic disorders and possibly in inanition. Mild hepatic changes have been found in a few patients with idiopathic hypoproteinæmia, but these patients and others with this disease have shown no clinical signs of hepatic disease. Although it sounds improbable, the hypothesis that an entirely unknown liver disease with reduced protein synthesis caused the hypoproteinæmia was accepted until a few years ago.

Inanition may be ruled out. As a rule the patients have received good nutrition, and therapeutic experiments with high-protein diets have given consistently negative results.

External protein loss through the kidneys, skin, or respiratory tract has never been demonstrated in these patients. Fæcal nitrogen loss has not been observed; and, where nitrogen balance has been tested, this has been positive.

The last possibility—increased internal protein loss—was suggested as early as 1935 by Cope and Goadby.[7] At that time this explanation was regarded as improbable, but this view has been altered by recent studies.

By metabolic studies following infusions of albumin in a case of idiopathic hypoproteinæmia, Albright et al. (1949)[1] showed that the basic defect was increased destruction of protein, and in 1950 Kinsell et al.,[24] using labelled aminoacid, made the same finding.

By means of ^{131}I-labelled albumin this feature was demonstrated in one of our patients.[35] Subsequently, we have studied two further patients with idiopathic hypoproteinæmia [36]; and by the same technique Corbeel et al.,[8] Thorn et al.,[39] and Cattel and Norris [5] have investigated one patient each. In all cases the result was the same: the patients broke down and synthesised not little but much albumin, and in relation to the total and circulating albumin the turnover was rapid. There is thus a question of hypercatabolism.

These investigations did not solve the mystery, but by proving that the albumin synthesis is normal they showed that the hypoproteinæmia must be due, not to reduced synthesis, but to a loss of protein. Consequently, further investigations must be concentrated on detecting the cause of this loss which must take place within the organism.

A year ago Citrin et al.[6] reported a case of hypertrophic gastritis associated with hypoproteinæmia and œdema. They found that a fluid containing protein oozed into the stomach, and by means of ^{131}I-labelled albumin they showed a pronounced loss of albumin in the stomach and a rapid turnover of the small albumin pool. Owing to severe loss of albumin in the stomach, the patient had hypoproteinæmia. Citrin et al. did not relate their very important finding to idiopathic hypoproteinæmia, but their observation showed clearly that serum-albumin may be lost in the gastrointestinal tract.

While albumin is demonstrable directly in the gastric juice, at least in certain cases,[6] the position is complicated if large quantities of proteolytic enzymes are present, as they usually are, in the stomach and intestine. In that event, labelled albumin will be degraded to aminoacids, and the labelling substance (^{131}I) will be absorbed and excreted in the urine. There will be no increase in the fæcal excretion of ^{131}I—representing a loss of albumin into the lumen of the alimentary organs—and in a metabolic study such albumin catabolism will be recorded as "internal". Then we are back again where we started.

An elegant evasion of the enzymatic protein breakdown in the gastrointestinal tract has been advocated by R. S. Gordon who labelled the well-known artificial plasma substitute polyvinyl pyrrolidone (P.V.P.) with ^{131}iodine. This synthetic polymer is unaffected by the proteolytic enzymes, and after injection into the blood-stream in a suitable molecular size abnormally large quantities of ^{131}I should be demonstrable in the fæces, if there are "leakages" in the gastrointestinal tract.

During the past six months we have studied several patients suffering from idiopathic hypoproteinæmia with ^{131}I-labelled P.V.P. made by Gordon in U.S.A. and supplied to us for these investigations. In addition to a series of normal persons, we have so far investigated four patients with idiopathic hypoproteinæmia using P.V.P. as well as ^{131}I-labelled albumin.

Methods

^{131}I-labelled albumin was prepared by the method of Veall et al.[40] For each investigation, we used about 25 mg. albumin with an activity of 30–50 μC. The albumin turnover was calculated partly according to Sterling's [37] method (cases 1–3) and partly by the method of Pearson et al.[31] (case 4). ^{131}I-P.V.P. was produced by R. S. Gordon [149] (National Institutes of Health, Bethesda, Md, U.S.A.) and posted by air to Denmark. Four different P.V.P. preparations were used. P.V.P. was administered intravenously in quantities of 1–18 ml. in an approximately 0·2% solution, with an activity of 20–30 μC. According to Gordon the molecular size averages 40,000. After the injection, the radioactivity was controlled in daily plasma specimens, and the excretion in the urine and fæces was also controlled daily. All specimens were counted with a scintillation counter. One or more normal subjects were investigated by all preparations of ^{131}I-albumin and ^{131}I-P.V.P.

Findings

The histories and the most important findings in the four cases of idiopathic hypoproteinæmia were as follows:

Case 1.—A man, aged 34, with varying dependent œdema of 3 years' duration, but no other complaints; not dyspeptic. He had been admitted 18 months previously for investigation of the œdema. His total serum-protein was about 4 g. (albumin 2 g.) per 100 ml. The œdema was due to the hypoproteinæmia, but the cause of the hypoproteinæmia could not be demonstrated. Injection of ^{131}I-labelled albumin showed very quick

SERUM-PROTEINS, ALBUMIN DEGRADATION, ^{131}I-P.V.P. EXCRETION, AND FÆCAL NITROGEN IN FOUR PATIENTS WITH IDIOPATHIC HYPOPROTEINÆMIA AND ONE WITH STEATORRHŒA (SPRUE)

Diagnosis	Case no.	Age (yr.)	Sex	Serum-protein (g. per 100 ml.)			Total albumin (g./kg.)	Intravascular albumin (g./kg.)	Albumin degradation (g./kg./day)	^{131}I-P.V.P. test †	Fæcal nitrogen (g./day)
				Total	Albumin	Globulin					
Idiopathic hypoproteinæmia..	1	34	M	4·31	2·17	2·14	3·66	1·35	0·385	3·41	1·25–1·69
„ „ ..	2	30	F	4·8	2·45	2·35	2·08	0·98	0·339	4·14	..
„ „ ..	3	28	F	4·3	3·01	1·29	3·80	1·30	0·366	3·14	0·84–0·89
„ „ ..	4a	62	M	4·72	2·61	2·11	5·38‡	1·14	0·319‡	4·76	0·56–1·00
	4b*			6·24	3·78	2·46	5·56	1·87	0·149	1·03	..
Steatorrhœa	..	38	M	5·12	2·74	2·38	2·65	1·46	0·428	7·95	2·22–3·14
Normal persons	..	..	..	6·2–7·6	3·9–4·9	2·2–3·0	3·55–5·05	1·61–2·87	0·175–0·243	0·18–1·03	1·3±0·5

* After partial gastrectomy.
† Fæcal excretion in 5 days, as % of amount injected.
‡ Examined after albumin infusion.

turnover (see accompanying table). Examination of liver, kidneys, and heart revealed no abnormalities. The only abnormal finding was severe, diffuse, hypertrophic gastritis demonstrated by X-rays and gastroscopy. The condition was diagnosed as idiopathic (hypercatabolic) hypoproteinæmia. The patient soon discharged himself against medical advice, but he was readmitted in the spring of 1958 in very poor condition. He had developed monstrous œdema, and in the past few months also diarrhœa. Total serum-protein was now 4·6 g. per 100 ml., but the albumin fraction was only 0·8 g. per 100 ml. On admission, his condition was characterised by generalised œdema, including ascites.

Investigations showed no further abnormalities, and X-rays of the stomach again revealed typical hypertrophic gastritis (fig. 1). With Citrin's patient in mind, it was assumed that this was the cause of his trouble and that he was losing large quantities of protein, especially albumin, in the stomach. But, despite several attempts, it proved impossible to find albumin in the gastric juice, presumably because it was digested too quickly.

Examination with ^{131}I-P.V.P. showed a greatly increased excretion in the fæces (9 times that in a normal subject studied at the same time) as is apparent from the table and fig. 2. There was clearly pronounced leakage in the gastrointestinal tract; and it was concluded that the rational treatment was operation, removing as much as possible of the site of leakage—the stomach.

Fig. 1—Radiograph of stomach in case 1, showing hypertrophic gastritis.

Extensive partial gastrectomy was carried out in surgical department A (Dr. K. H. Køster). The specimen showed changes which were grossly as well as microscopically characteristic of hypertrophic gastritis (figs. 3 and 4).

Biopsy specimens from the duodenum and jejunum exhibited an entirely normal mucosal pattern, but several of the muscle cells of the external muscularis layers included large quantities of peculiar granules (hæmofuchsin?) evidently similar to those found previously in certain cases of sprue [18] (fig. 5). At present we cannot interpret the significance of this finding.

The postoperative course was stormy, with several episodes of pulmonary œdema and pneumonia. When the condition was thought to have been stabilised and the patient had just been allowed out of bed, he suddenly died. Necropsy revealed severe pulmonary œdema. All organs were examined, but apart from the pulmonary œdema there were no noteworthy changes. The operative site was as might be expected. The most important laboratory data are shown in the accompanying table.

Case 2.—A woman, aged 30, who had had mild bronchial asthma since childhood. For the past 15 years she had had

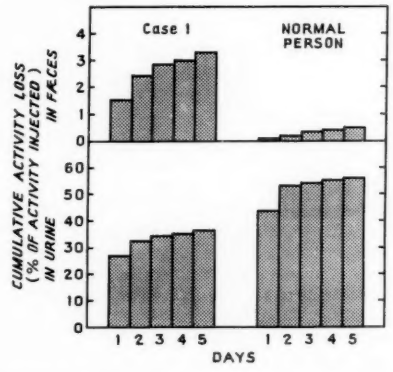

Fig. 2—^{131}I-P.V.P. excretion in fæces and urine in case 1 and normal person.

hypoproteinæmia, the severity of which had varied, with a corresponding varying tendency to œdema, often associated with ascites. In these 15 years she had been examined in many hospitals, but the cause of the hypoproteinæmia, total serum-protein about 4–5 g. (albumin 2–3 g.) per 100 ml. had not been detected. Besides asthma and œdema she had intermittent diarrhœa and nausea; but otherwise her general health had been good, and she had not lost weight. Five years previously, repeated X-ray investigations in another hospital had shown abnormal appearances of the small intestine, a patchy dis-

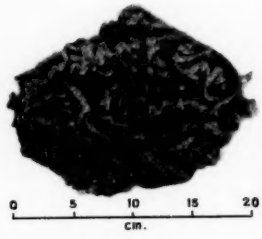

Fig. 3.

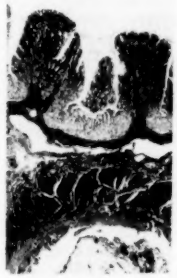

Fig. 4.

Fig. 3—Stomach from case 1 showing hypertrophic gastritis (partial gastrectomy).

Fig. 4—Microscopic picture of gastric wall from case 1 showing hypertrophic gastritis.

tribution of the opaque medium suggesting sprue. This investigation had been repeated several times within the past year, but no abnormality had then been found.

Investigation of the albumin turnover with ^{131}I-albumin revealed a very rapid turnover of a small pool (see accompanying table). Injection of ^{131}I-P.V.P. gave an excretion of 4·1% in the fæces (see accompanying table).

In view of these findings it was assumed that the protein loss took place in the small intestine; but, in the hope that the process was localised enough for resection to be usefully performed, laparotomy was undertaken.

Fig. 5—Biopsy specimen of jejunum in case 1, showing much granular pigment (hæmofuchsin?) in muscularis.

Despite normal X-ray appearances immediately before the operation, severe changes were found throughout the small intestine. The wall was darkly pigmented; it was œdematous with a distinct lymphatic pattern. In the œdematous mesentery there were numerous lymph-nodes enlarged to the size of hazel nuts. Although the changes were most severe in the proximal portion, resection of a large segment of the intestine was considered too formidable an intervention with too little prospect of success. The patient stood the operation well, but her condition is unchanged. Microscopic examination of a biopsy specimen of jejunum showed, in this case too, many granules in the cells of the muscularis, but no mucosal changes.

Case 3.—A woman, aged 28, who had been ill for at least 9 years. The only sign was constant œdema of the lower limbs, and now and then of the hands and face too. Apart from the œdema she was fit, and she was working. Periodically she had vague dyspeptic complaints in the form of nausea and sense of pressure in the abdomen after meals, but never vomiting or diarrhœa. The serum-protein was fairly constant—4–5 g. (albumin 2–3 g.) per 100 ml. This case has been reported by Schwartz and Thomsen.[35] Her disease was diagnosed as hypercatabolic hypoproteinæmia. Investigation with ^{131}I-P.V.P. showed increased fæcal excretion (see accompanying table). Repeated X-ray investigations of the gastrointestinal tract had shown no abnormality. In 1955 and 1958 the X-ray appearances were suggestive of jejunitis, but the changes were very slight. After the P.V.P. test we are in no doubt that the site of protein loss is the gastrointestinal tract—more accurately the small intestine. Exploratory laparotomy is planned, although neither the patient nor we expect that it will prove very successful.

Case 4.—A man, aged 62, with well-controlled diabetes mellitus of several years' duration. A year before admission he rather suddenly developed dyspeptic complaints in the form of anorexia and vomiting and lost 12 kg. At another hospital he was treated for pyloric gastritis by an ulcer regime, and the symptoms of dyspepsia disappeared almost entirely.

A few months later he began to have dependent œdema, which has persisted ever since. The cause of this œdema was severe hypoproteinæmia, the total serum-protein being about 5 g. (albumin about 2·5 g.) per 100 ml. No explanation of the hypoproteinæmia was discovered; liver, kidneys, and heart were normal. Since the case was entirely obscure, exploratory laparotomy was performed; apart from mild ascites, this did not reveal any abnormality.

Three months later the patient was transferred to the University Hospital, medical department A. Investigations in this department again showed no abnormality except for the low serum-protein level and X-ray evidence of quite severe hypertrophic gastritis.

The patient was transferred to Bispebjerg Hospital, Medical Department B, to be investigated for protein loss in the stomach.

Aspiration of gastric juice, from the fasted and histamine-stimulated stomach, gave the results shown in fig. 6.

It is evident that the fasting gastric juice contained considerable quantities of albumin, which was immediately digested upon stimulation. The albumin content of the gastric juice ranged from 0·4 to 0·8 g. per 100 ml. in repeated tests. If the daily secretion is estimated as $1^1/_2$–2 litres, a rough calculation shows that the patient may lose about 10 g. albumin a day by this route.

Albumin degradation, measured by ^{131}I-labelled albumin, was found to amount to 20·0 g. (0·319 g. per kg. body-weight) per twenty-four hours—a fairly high value, but not sufficient to compensate for the great loss in the stomach. The ^{131}I-P.V.P. excretion in the fæces was 4·8% of the injected dose—i.e., considerably increased (see table). Extensive partial gastrectomy was carried out at the University Hospital surgical department D (Dr. M. Andreasen).

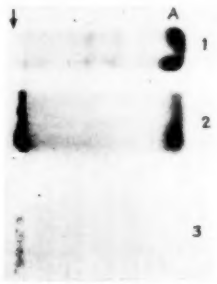

Fig. 6—Paper electrophoresis in case 4 of: (1) serum, (2) gastric juice before histamine stimulation, and (3) gastric juice after histamine stimulation.

The removed stomach exhibited typical hypertrophic gastritis, grossly and microscopically. Biopsy of the jejunum did not show granules in the cells of the muscularis.

The postoperative course was uneventful, and the patient has been fit ever since. Four weeks after the operation the serum-albumin level had risen to near-normal (see accompanying table), and the œdema has disappeared. Three months after the operation the P.V.P. test was repeated and was now in the normal range.

Discussion

External protein loss was demonstrable in none of these four cases. Albumin synthesis, in terms of the degradation of ^{131}I-labelled albumin, was high (hypercatabolic) in all cases compared with normal persons (see accompanying table).

Low serum-albumin in a patient with high albumin synthesis in whom external loss can be ruled out must denote an internal loss of albumin. In case 4, with hypertrophic gastritis, considerable loss of albumin in the stomach was directly demonstrable; and in all four cases the fæcal excretion following intravenous injection of ^{131}I-P.V.P. was abnormally great, indicating leakage of colloids into the gastrointestinal tract. Two of our patients had hypertrophic gastritis and the other two a disease of the small intestine whose ætiology remains unelucidated. In all cases the main sign had been œdema, and dyspeptic complaints had been slight or absent.

In thirty-one reported cases of idiopathic hypoproteinæmia [2 3 5 7–13 15 17 19 21–23 25–27 30 32–35 38 39 42] we have found data regarding investigation for and signs of gastrointestinal disturbances. In no less than fourteen cases [2 3 9–12 15 19 22 23 28 29 33 39] the complaints had been quite severe, in most cases severe diarrhœa; and at least three [9 11 29] of the reported cases had hypertrophic gastritis. Invariably these signs were regarded as of no significance in relation to the main disease, or else they were thought to be secondary to the hypoproteinæmia. Because of the present findings, we believe that gastric or intestinal disease may be the basic trouble in some of these cases. The concept of idiopathic hypoproteinæmia can apparently be at least restricted, and whether it will disappear entirely the future will decide. In our cases the hypoproteinæmia has proved to be a sign of a disease, but a sign which has predominated to the extent of obscuring this disease.

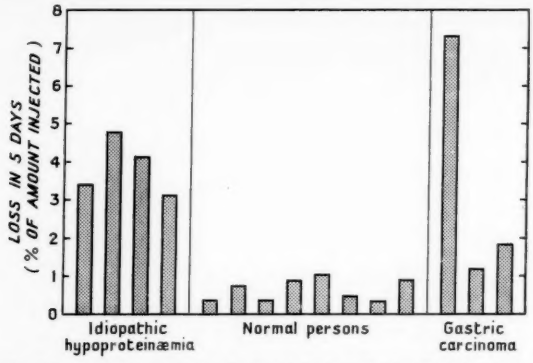

Fig. 7—^{131}I-P.V.P. excretion in fæces in 4 patients with idiopathic hypoproteinæmia, 8 normal persons, and 3 patients with gastric carcinoma associated with hypoproteinæmia.

The term hypercatabolic hypoproteinæmia describes an essential aspect of the protein (albumin) turnover in these cases. The albumin turnover is high, relatively and to some extent also absolutely. In other words these patients produce as much albumin as they can, but the ability of the liver to synthesise albumin is fairly restricted, and it is unable to synthesise the extra quantity needed.

Hypoproteinæmia due to protein loss in the gastrointestinal tract may also be associated with other diseases. It is well known that cancer of the stomach may be accompanied by hypoproteinæmia, and we have therefore included such patients in our ^{131}I-P.V.P. studies. Fig. 7 sets out the results of this test in three patients. The patient with a fæcal excretion of 7% had a widespread inoperable cancer, and his serum-protein was 5·5 g. (albumin 2·01 g.) per 100 ml. Electrophoretic studies of the gastric juice revealed free albumin. The hypoproteinæmia was not due to hæmorrhage, and the most likely explanation seems to be that the disorder is analogous to that in hypertrophic gastritis.

Future studies may reveal whether the hypoproteinæmia commonly associated with sprue is of the same genesis—being due to protein loss in the intestine instead of malabsorption, as is generally assumed. We have studied only one case, and in this patient there was an extremely great ^{131}I-P.V.P. excretion and much hypercatabolic albumin degradation (see accompanying table), but further cases must be studied.

Another factor which remains unelucidated is the actual cause of the oozing of protein. It is not known whether this is due to capillary leakage or to a mucosal defect—or to both. So far, pathological investigations have not yielded definite information.

Summary

In four cases of so-called idiopathic hypoproteinæmia there was high albumin degradation (hypercatabolism), and radioactive polyvinyl pyrrolidone revealed pronounced permeability to high-molecular substances in the gastrointestinal tract.

The hypoproteinæmia was due to loss of protein in the lumen of the gastrointestinal tract, constituting a sign of disease in this system (hypertrophic gastritis, disease of the small intestine). In other gastrointestinal diseases involving hypoproteinæmia (cancer of the stomach, sprue), this sign may be of the same genesis.

We wish to thank Dr. R. S. Gordon for his generous supplies of ^{131}I-P.V.P. and also for his suggestion that the substance should be used in idiopathic hypoproteinæmia; and Prof. K. Brøchner-Mortensen, Dr. M. Bjørneboe, Dr. P. Lous, Dr. H. Heckscher, Dr. K. H. Køster, and Dr. M. Andreasen for their interest and help. This study was supported by grants from Statens Videnskabsfond and Kong Christian Den Tiendes fond.

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Addendum

At laparotomy in case 3 the findings were almost identical with those in case 2, with dark pigment in the upper two-thirds of the small intestine and large quantities of pigment granules in the muscular cells.

MILKBORNE STREPTOCOCCAL SORE THROAT

A STUDY OF 835 CASES

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OPPORTUNITIES to study large foodborne epidemics of streptococcal respiratory diseases have been relatively few.

In three similar epidemics at Akrotiri, a large R.A.F. station in Cyprus, in the summer of 1957, 835 cases of tonsillitis or pharyngitis were admitted to hospital. There were 120 cases of scarlet fever amongst them. The causative organism was the hæmolytic streptococcus and the source of the primary cases is believed to have been milk.

Investigation and Treatment

The patients, young airmen living on the station, were examined before admission, and a throat swab was taken and plated out on human blood agar. Oral temperature was recorded at four-hourly intervals until it had been normal for twenty-four hours and then twice daily. All patients were examined daily and were discharged when they were symptom-free, afebrile, and had a clean throat. On discharge from hospital a throat swab was taken and urine examined for protein; these investigations were repeated at weekly intervals for a further two weeks.

Throughout the three epidemics, subcultures of the β-hæmolytic streptococci were made in every case to assess the sensitivity of the organism to penicillin and sulphafurazole. All 587 positive cultures from the first two epidemics were grouped by Lancefield's tube technique and bacitracin sensitivity. 19 random cultures in nutrient broth were sent to the Streptococcal Reference Laboratory for grading and typing.

A controlled therapeutic trial was impossible in the first two epidemics, but this was achieved in the third (McDonald and Taylor 1958). In all, 336 patients received 'Sulphatriad' tablets (sulphadiazine, sulphamerazine, and sulphathiazole) (4 g. followed by 1·5 g. four-hourly) with soluble aspirin; 99 patients received penicillin either parenteral (500,000 units six-hourly) or oral 'Distaquaine V' (120 mg. eight-hourly) with soluble aspirin; and 383 patients received soluble aspirin alone. All patients remained in bed until their temperature had been normal for at least twenty-four hours.

Epidemiology

The three waves began on May 12, May 26, and Aug. 3 (fig. 1) and all showed the same pattern. The explosive start suggested a foodborne infection.

All patients were living-in airmen eating in one mess; no officers, senior N.C.O.s, or living-out personnel were affected. Many patients had not been to the NAAFI but they all had eaten in the airmen's mess. There were no cases from the neighbouring signals unit, which had its own mess, although those men spent much of their off-duty at the main camp NAAFI and cinema. Breakfasts were the only meals which all the patients had attended and milk in tea or on cereals was the only common food.

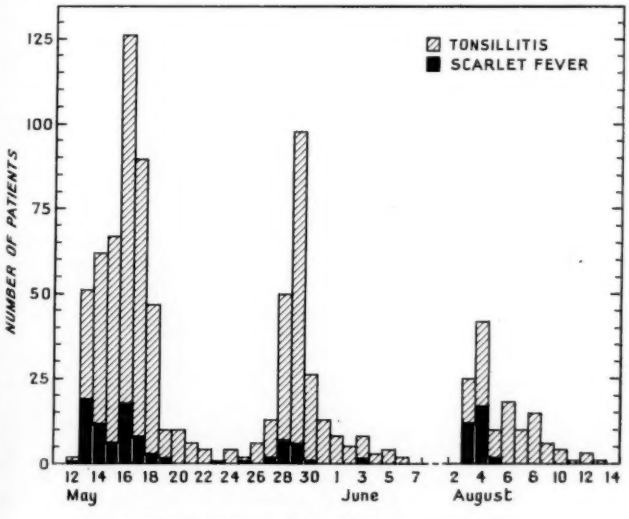

Fig. 1—Daily incidence of tonsillitis and scarlet fever.

By the third epidemic it was realised that the three outbreaks had come at intervals of multiples of a fortnight and that an explosive outbreak of 127 cases of acute gastroenteritis among the airmen on March 30 fitted into this pattern. In all four epidemics the first cases appeared during the weekend after the fortnightly pay parade. This was the important clue.

After pay parade the number on duty as night staff of the airmen's mess was reduced from four to three, and they were often interrupted by convivial airmen demanding snacks. Furthermore, the mess was used for tombola on these nights, providing another distraction.

All milk consumed in Akrotiri is tinned milk diluted with water. The kitchen regulations stipulated that milk should not be prepared until just before breakfast at 5.30 A.M. and that it should be kept in covered containers. But two cooks admitted that on these fortnightly pay nights, because of pressure of work later in the night, they often made up the milk at midnight and that it was often sampled thereafter.

All the airmen's mess staff had their throats swabbed on May 14 and this yielded 12 positive cultures of group-A streptococci out of 64 persons. None of the night duty staff was positive, but nasal swabs were not taken. The convivial intruders could not, of course, be traced.

These findings seem compatible with milk being the vehicle of infection.

Clinical Features

The illnesses were essentially similar to those previously described (Gardner 1952, Chapple et al. 1956). There were few complications and the great majority of patients recovered rapidly.

The illness began abruptly with malaise or sore throat and almost all patients were admitted within twenty-four hours. Considerable injection of the throat was the rule with a variable amount of œdema, and purulent exudates were seen in all with intact tonsils. Tender cervical glands were also present and persisted for a week or so after the other signs had gone.

120 patients had the characteristic punctate erythema of scarlatina, usually only moderate in severity, and bearing no relation to the degree of prostration. The rash appeared on the third day of illness in 60% of cases and on the second day in only 28%. The daily incidence of scarlet fever is shown in fig. 1.

Epistaxis, reported by Glover and Griffith (1931) in more than a third of their cases of airborne tonsillitis, was found in only 2 patients. Cough, nausea, and vomiting were not noticeable.

The severity of the illness was much greater in the first two days of each wave.

Laboratory Findings

Of the 754 whose throats were swabbed on admission, 432 were found to carry group-A *Streptococcus pyogenes*. All twelve representative subcultures from the first two waves sent to the Streptococcal Reference Laboratory belonged to Griffiths type 5/12/27 while the seven subcultures from the third epidemic were found to belong to either Lancefield groups A or G.

All positive cultures were sensitive to penicillin and sulphafurazole, and resistant strains of the organism did not appear. In every case there was complete agreement between the standard tube-grouping technique and the simpler bacitracin sensitivity method for determination of Lancefield's group A.

Leucocyte-counts performed on the first 35 patients on May 13, few of whom had been ill for more than forty-eight hours, showed a wide variation of neutrophil response: these varied

from 7200 per c.mm. (60% neutrophils) to 25,000 per c.mm. (92% neutrophils). Of these 86% had a total white-cell count greater than 10,000 per c.mm.

The erythrocyte-sedimentation rate was also measured on these patients and varied from 2 to 71 mm. in one hour (Westergren), 83% having a reading above 5 mm. in one hour.

Positive Swabs after Treatment

In all three waves 19·6% of patients had a positive throat swab when they had recovered clinically. Although it is impossible to make a fine comparison of the effects of treatment since the majority of cases were selected, the breakdown of the carrier-rate reveals noteworthy differences: penicillin (99 cases) carrier-rate 1%, sulphatriad (336) 14%, aspirin (383) 24%. The final carrier-rate two weeks after discharge from hospital for all patients was 4·7%.

Complications

Secondary adenitis.—4 airmen were readmitted with fever and acutely swollen tender cervical glands between twelve and twenty-three days after the original admission. In all 4 the tonsils were only mildly injected and the throat swab was normal.

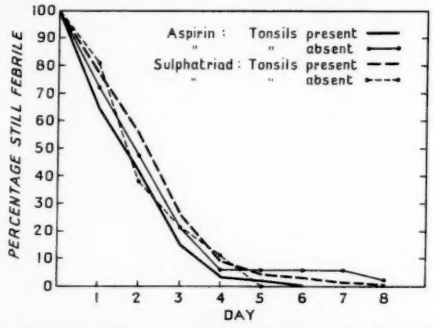

Fig. 2—Duration of fever in sulphatriad and aspirin groups was not apparently related to a history of tonsillectomy.

All were treated with crystalline penicillin and remained in hospital for from four to twelve days. During their initial admission 2 had had aspirin only, 1 sulphonamide, and 1 penicillin.

Otitis media.—There were only 5 cases of acute otitis media (less than 0·6%). 4 cases settled without perforation, and the 5th perforated within a few hours of admission.

Acute nephritis.—The three weekly examinations of urine after discharge from hospital were undertaken with this complication in mind. Only 3 mild cases were found. The periods between admission with tonsillitis and readmission with nephritis were eight, nine, and thirteen days. 2 of the patients had received sulphatriad and one aspirin.

Rheumatic fever.—Not one case of rheumatic fever appeared in the total of 835 cases. In June, however, an airman was admitted with typical acute rheumatic fever. He had been on the station during the first two epidemics, the second of which was just three weeks before his admission, but he had not suffered from a sore throat at the time.

Gastrointestinal disturbances.—20 patients developed gastrointestinal symptoms during their stay in hospital of whom 1 had Sonne dysentery and 6 had a bacillary exudate in their stools. These were probably coincidental as dysentery is endemic in Cyprus.

TABLE I—MAXIMUM TEMPERATURES

Temperature	With Tonsils	Without Tonsils
Below 99°	57 (9·2%)	11 (7·3%)
99–100	132 (21·2%)	20 (13·2%)
100–101	115 (18·5%)	31 (20·5%)
101–102	100 (16·1%)	38 (25·2%)
102–103	119 (19·2%)	31 (20·5%)
103–104	72 (11·6%)	18 (11·9%)
104 and above	26 (4·2%)	2 (1·3%)
Totals	621	151

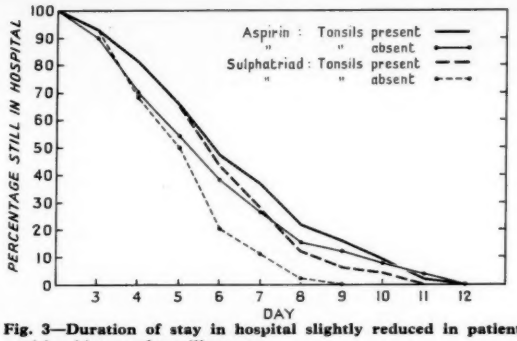

Fig. 3—Duration of stay in hospital slightly reduced in patients with a history of tonsillectomy.

Secondary monilial infection.—4 patients, all of whom had a positive throat swab on admission, developed a secondary monilial infection of the throat. 3 had had penicillin and 1 aspirin.

Effect of Tonsillectomy

Soon after the first epidemic began we decided to ask all patients whether they had had a tonsillectomy. 795 patients were questioned, and of these 158 (19·8%) said they had had the operation. A later survey of 218 airmen who were at risk but who had not been ill produced 81 (37·2%) whose tonsils had been removed.

In a later random survey of 500 airmen on the station, the incidence of tonsillectomy was found to be 32%. This figure is almost identical with the 31·9 among 1434 R.A.F. recruits (Carne 1956).

Tonsillectomy seems to be associated with a lowered susceptibility to food-borne tonsillitis, although it is conceivable that tonsillectomy provides a striking degree of protection against this disease.

Severity of illness was assessed by fever and the length of stay in hospital. Since the treatment of patients in the first two waves was selective, one can only compare these factors within the treatment groups, but fortunately both the sulphatriad and aspirin groups were very large. Comparison of both height and duration of fever revealed no significant difference (table I, fig. 2).

TABLE II—ATTACK-RATES IN GROUPS AT RISK

—	First epidemic	Second epidemic			Third epidemic		
—	—	Ill in first epidemic	Not ill in first epidemic	New arrivals	Ill in first or second epidemic	Not ill in first or second epidemic	New arrivals
At risk	2121	411	1512	52	654	1274	197
Attacked (Attack rate)	483 (22·8%)	64 (15·6%)	164 (10·8%)	8 (15%)	18 (2·8%)	53 (4·2%)	45 (22·8%)

On the other hand there was a slight but definite reduction in time of stay in hospital in those patients with a history of tonsillectomy, although this did not become significant until the 7th day (fig. 3). This may be explained by the fact that a clean throat was one of the criteria for discharge and purulent exudates were not so evident in patients with little or no tonsillar tissue.

Immunity to Tonsillitis

The figures were examined for evidence of protection in subsequent epidemics as a result of clinical illness. Table II shows attack-rates in groups at risk, allowing for movement of airmen in and out of the station.

There was apparently no significant immunity in persons exposed in the second wave who had been ill in the first, but there was a striking immunity conferred on those exposed in the third wave two months later, though the attack-rate among the new arrivals was as high as it had been in the first wave. It therefore seems that significant immunity to streptococcal infection takes more than two weeks to develop. A study of the 64 cases of reinfection in the second wave showed that treatment bore no relation to the chances of reinfection and this also applies to those reinfected in the third wave.

Discussion

We have traced descriptions of four explosive foodborne epidemics of streptococcal tonsillitis in the past fifteen years (Bloomfield and Rantz 1943, 341 cases, Wilson 1944, 89 cases, Commission on Acute Respiratory Diseases 1945, 100 cases, and Gardner 1952, 265 cases).

Such epidemics differ from the more common airborne outbreaks by their abrupt onset, sudden termination, and low complication rate. It has been suggested that these characteristics are produced by a massive infection with a relatively avirulent organism.

Outbreaks of this kind in Service communities mean that a unit may become useless with dramatic suddenness In the Akrotiri epidemics over 5000 man-days were lost through time in hospital, and in addition about a further 3000 days in sick leave.

The low incidence of complications in this series accords with other reports of foodborne epidemics. Rammelkamp et al. (1952) suggested that the proportion of streptococcal infections leading to rheumatic fever remains relatively constant between 2% and 4%. In this series there was only 1 case, agreeing with the findings of Gardner (1952) and contrasting with those of Henningsen and Ernst (1938) who reported 3% of rheumatic fever after a foodborne epidemic in Denmark.

Although rheumatic fever is apparently not associated with any particular type of group-A streptococci, acute nephritis is commonly associated with type 12 (Dingle et al. 1953). We found only 4 such cases in the first two epidemics in which streptococcus of type 12 had been found to be the causative organism, and they were mild and transient.

There was no case of " non-suppurative streptococcal fever " as described by the Commission on Acute Respiratory Diseases (1945).

Unfortunately, the first two outbreaks were so overwhelming that it was impossible to organise treatment on a non-selective basis. We are therefore unable to compare the results of the different methods of treatment. In the third epidemic in August, however, this was achieved and the results are described elsewhere (McDonald and Taylor 1958).

In this series we were able to make some assessment of the effect of previous tonsillectomy, and the results suggest that the operation is associated with a lowered susceptibility to infection, but once the illness is established the individuals fare no better than their intact brethren as judged by the height and duration of fever. Bacteriologically, however, there is a difference between the two groups since more patients with intact tonsils had positive throat cultures than those without tonsils. This supports the findings of other workers.

In the follow-up throat swabs perhaps the most noticeable feature was the remarkably low incidence of positives obtained of 4·7% two weeks after discharge.

Summary

Three epidemics of foodborne tonsillitis affected 835 young airmen, 120 of whom had scarlet fever. The cause in all three outbreaks was *Streptococcus pyogenes*. The evidence suggested that milk was the vehicle of infection.

The clinical features were similar to those in previously recorded foodborne epidemics, amd there were few complications. There was a much lower susceptibility to the disease in patients with a past history of tonsillectomy.

We wish to thank the Director-General of the Royal Air Force Medical Services for permission to publish; and all those medical officers and laboratory technicians at Akrotiri whose hard work formed the backbone of the paper, and particularly Wing-Commander R. Mortimer, of the R.A.F. Institute of Pathology and Tropical Medicine, who gave great help in elucidating the epidemiology. We should also like to thank Dr. R. E. O. Williams, of the Streptococcal Reference Laboratory, and Dr. J. C. McDonald, of the Public Health Laboratory Service, for helpful advice and criticism in the compilation of the paper.

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DETERMINATION OF PLASMA-VOLUME USING INTRAVENOUS IRON DEXTRAN

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ESTIMATION of blood-volume in human subjects depends on establishing, first, the proportion of cells to plasma, and, secondly, either the plasma-volume or the cell-volume. The total cell-volume can be measured with radioactive tracers ^{32}P (Reeve and Veall 1949) or ^{51}Cr (Verel et al. 1956), but these techniques are limited to the larger hospitals with suitable facilities. In smaller hospitals volume studies depend on estimating either the red-cell volume by differential agglutination (Ashby 1925, Barnes et al. 1948) or, more usually, plasma-volume with the dye Evans-blue, T1824 (Gibson and Evans 1937, Mollison 1951).

Over the past fifty years volume studies have been made by other methods (Rowntree et al. 1929, Mollison 1951), but these have been unsatisfactory and the Evans-blue method has some disadvantages.

We consider that plasma-volume can be estimated quickly and accurately by the intravenous injection of

TABLE I—OPTICAL DENSITIES OF STANDARD IRON SOLUTIONS 10 MM. CELLS: FILTER ILFORD GREEN 624

—	Ml. of standard iron solution					
	0·5	1·0	1·5	2·0	2·5	3·0
µg. Fe	1·4	2·8	4·2	5·6	7·0	8·4
Optical density ..	0·095	0·185	0·28	0·37	0·47	0·55
Equivalent to µg. Fe per 100 ml. plasma ..	420	840	1260	1680	2100	2520

iron-dextran complex (' Imferon ', Benger). This substance is marketed for intramuscular injection in the treatment of iron deficiency anæmia, but there is no contra-indication to its intravenous administration. Owing to its large molecular structure it is not quickly removed from the circulation; it is neutral, isotonic, and virtually non-irritant. Each millilitre of imferon contains the equivalent of 50 mg. elemental iron; the intravenous injection of 1 ml. will therefore give a circulating level of iron in plasma of between 1500 and 2000 µg. per 100 ml. in the average adult. The circulating iron can be measured easily and accurately in about thirty minutes using as little as 0·5 ml. plasma.

Method

5 ml. blood is removed from one arm (sample A). This can be allowed to clot or can be put in heparin or oxalate but not in ' Sequestrene '. 1 ml. imferon is injected slowly through the same needle using a tuberculin syringe, with a to-and-fro motion of the plunger. 15 minutes after the injection 5 ml. blood is removed from the other arm (sample B).

The circulating iron is estimated by a simplified modification of the method described by Trinder (1956). Centrifuge tubes should be of hard glass and rendered iron-free by any of the accepted methods.

Reagents

1. Sodium acetate ($C_2H_3O_2Na\ 3H_2O$) 40 g. per 100 ml. w/v.
2. Trichloracetic acid (T.C.A.) 20 g. per 100 ml. w/v.
3. Standard iron (2·8 µg. Fe per ml.). Ferrous ammonium sulphate 1 ml. 0·01*N* in 0·1*N* sulphuric acid, diluted to 200 ml. with water.
4. Thioglycollic acid.
5. Iron reagent. Sulphonated 4 : 7 diphenyl 1 : 10 phenanthroline (Trinder 1956).

All reagents keep indefinitely in ' Pyrex ' glass bottles.

TABLE II—RECOVERY OF KNOWN AMOUNTS OF IRON FROM POOLED PLASMA: RESULTS EXPRESSED AS µG. PER 100 ML.

Imferon added to plasma	Imferon recovered from plasma	Percentage recovery
500	510	102
1000	990	99
1500	1530	102
2000	1995	99·8
2500	2505	100·2

Procedure

0·5 ml. plasma or serum is pipetted into a 15 ml. centrifuge tube; 4 ml. water, 1·5 ml., T.C.A., and 0·05 ml. thioglycollic acid are added and mixed by lateral shaking. The tube is heated in a water-bath at 90–95° C for 10 minutes, and the contents are mixed after 3 and 6 minutes by gentle shaking. The tube is then spun at 4000 r.p.m. for 5 minutes, and 4 ml. clear supernatant fluid is pipetted into another tube. 0·4 ml. iron reagent and 0·6 ml. 40% sodium acetate are then added, mixing after each addition. Using a photoelectric colorimeter with 1 cm. cells and green Ilford filter 624 the instrument is set at zero using sample A; the reading of sample B is then taken.

The iron content of sample B can be obtained from a graph previously prepared with a series of iron solutions. These are made from the standard iron solution using 0·5, 1, 1·5, 2, 2·5, and 3 ml. quantities, 1 ml. T.C.A., and making each up to 4 ml. with water. After adding 0·05 ml. thioglycollic acid and heating at 90–95° C for 10 minutes, 0·4 ml. iron reagent and 0·6 ml. 40% sodium acetate are added as before. The colour densities are read as before on the photoelectric colorimeter, the colorimeter blank being prepared with 3 ml. distilled water and 1 ml. T.C.A. treated in the same way. The optical densities of these amounts of iron are shown in table I; when the optical densities are plotted against the iron content of the solutions a straight-line graph is obtained. When the quantity of iron in sample B is known the plasma-volume is calulated thus:

$$\text{Plasma volume in ml.} = \frac{50{,}000}{\text{Iron content of sample B in µg. per ml.}}$$

Results

Recovery experiments were carried out by adding known amounts of imferon to pooled plasma. The results expressed in table II show that the recovery was quantitative.

The suitability of any substance used for volume studies depends on its remaining in the circulation long enough to allow proper mixing in the body: it must not be removed rapidly by excretion or by tissue fixation. To demonstrate the rate of elimination of imferon from the circulation 18 patients were given 1 ml. intravenously and the plasma-iron levels were estimated at intervals up to 2 hours (table III). In the 2 hours following injection it appears that an average of less than 10% of iron is lost from the circulation. This is similar to the rate of removal of Evans-blue dye from the circulation (Noble and Gregersen 1946).

TABLE III—RATE OF ELIMINATION OF IMFERON FROM THE CIRCULATION IN 2 HOURS AFTER INTRAVENOUS INJECTION OF 1 ML.: RESULTS EXPRESSED AS µG. PER 100 ML.

Case	Min. after injection					Loss after 2 hr.	% loss in 2 hr.	Hb. (%)*
	15	30	60	90	120			
1	2355	2190	2100	2100	2100	255	10·8	110
2	2085	2085	..	1935	1890	195	9·3	103
3	2100	..	1920	1950	1920	180	8·6	104
4	1640	..	..	1600	1600	40	2·4	71
5	1950	1950	1854	..	1765	185	9·5	65
6	1800	1800	1680	1620	1575	225	12·5	90
7	1860	1680	1620	..	1620	240	12·9	110
8	1640	1560	1560	1550	1480	160	10·0	104
9	2145	2145	2010	..	2100	45	2·4	101
10	1935	1935	1770	1770	1680	255	13·3	94
11	2460	2370	2265	2205	2130	330	13·6	95
12	2640	2610	..	..	2430	210	8·0	96
13	1200	..	1170	..	1035	165	7·3	108
14	1830	..	1800	..	1665	165	9·0	102
15	1800	..	..	..	1650	150	8·3	115
16	1980	..	1920	..	1770	210	9·4	88
17	2175	..	..	..	2010	165	7·6	115
18	1770	..	..	..	1710	60	3·5	95

* 100% = 14·6 g. per 100 ml.

To find the rate of clearance of imferon from the plasma, the level of iron was estimated at 24, 48, and 96 hours after injection of 1 ml. intravenously (table IV). 48 hours after the injection, the level of iron in the circulation had decreased by 70–90%. After 96 hours the iron is almost entirely removed from the circulation. This is of practical importance because the plasma-volume estimation can be repeated accurately 48 hours after the first estimation.

Comparison of Results with Iron-dextran and Evans-blue

The plasma-volume of 12 healthy adults was estimated first by the iron-dextran technique, then 7–14 days later

TABLE IV—RATE OF CLEARANCE OF IMFERON FROM THE CIRCULATION AFTER INTRAVENOUS INJECTION OF 1 ML.: RESULTS EXPRESSED AS µG. PER 100 ML.

Case no.	Time of sample (hr. after injection)				Drop in 48 hr.	% drop in 48 hr.	Hb (%)*
	0·25	24	48	96			
1	1260	570	360	60	900	70·6	81
2	2235	870	210	0	2025	90	104
3	1980	855	360	0	1620	81	104
4	1870	790	310	130	1560	83	106

* 100% = 14·6 g. per 100 ml.

TABLE V—COMPARISON OF PLASMA-VOLUME USING IMFERON AND T1824: RESULTS EXPRESSED IN ML.

Case no.	Sex	Imferon	T1824	Difference of imferon from T1824
1	F	2200	2350	−150
2	M	2780	2850	−70
3	F	2400	2220	−20
4	F	2400	2350	+50
5	F	2350	2350	
6	M	2380	2590	−210
7	F	2300	2200	+100
8	F	1930	1940	−10
9	F	2300	2275	+25
10	F	2160	2200	−40
11	M	3225	3600	−375
12	M	2450	2500	−50

by a simple Evans-blue technique which Mollison (1951) and MacGregor and Tovey (1957) considered suitable for clinical use. The tests were made at the same time of day; none of the subjects were fasting (table v). Owing to persistent lipæmia no estimations by the Evans-blue technique were possible in 3 further subjects, though results were obtained with the imferon technique. Lipæmia renders the direct dye estimation with Evans-blue impossible. In 3 cases (2, 4, and 5) there was originally considerable discrepancy between the results obtained using the Evans-blue technique and the imferon technique. The estimations were repeated using both techniques, and comparable figures were obtained; but the results using imferon remained unaltered. The original results using Evans-blue were probably inaccurate owing to slight lipæmia. We consider that case 11 is typical of this discrepancy; the subject is a large man, but almost certainly the result using imferon is more near the truth than the result obtained with Evans-blue. As the subject left the area, repetition of both estimations was not possible.

The results using imferon do not tend to be higher than those obtained with Evans-blue: results significantly higher would suggest too rapid a removal of imferon from the circulation.

Discussion

All methods of measuring plasma or cell volume are open to criticism. The type of subject in whom volume studies would be most useful is often shocked, with collapsed veins, and may be losing blood at the time of study. Proper intravenous injection can thus be difficult, and loss of blood leads to erroneously high results. Using imferon, however, the test is as easy as with any other available technique; the small volume of fluid injected (1 ml.) can be measured with great accuracy in a tuberculin syringe; the markings are easily seen on the syringe.

A very real advantage of the imferon technique over Evans-blue is that standards do not have to be prepared each time an estimation is made: once the standard iron graph has been prepared this can be used until new reagents are necessary. Because of this advantage, only 5 ml. blood need be taken and the chemical estimation can be done in duplicate or triplicate.

The manufacturers claim that the iron content of each millilitre of imferon varies by as little as ±1·5 mg. per 100 ml.; commercial preparations of Evans-blue can vary very considerably.

Lipæmia does not in any way interfere with the imferon technique; it is the major source of error when using Evans-blue, and can be obviated only by techniques involving extraction of the dye from the plasma: even slight lipæmia renders the Evans-blue method inaccurate.

Finally from a purely technical point of view the estimation of iron is eminently satisfactory; the optical density of the "blank" is very low, while the optical density of the colour developed from the sample for iron estimation is in the range of maximum optical accuracy. With Evans-blue the "blank" is pure plasma—a substance which has considerable optical density.

The time taken from the injection of imferon to the final estimation of plasma-volume is about 50 minutes, allowing 15 minutes for mixing: no technique with comparable accuracy is faster.

The only precautions necessary with imferon are the avoidance of hæmolysis and the use of iron-free hard glass test tubes for the chemical estimation.

Conclusion

This new chemical technique for the estimation of plasma-volume depends on the estimation of iron in plasma after intravenous injection of 1 ml. iron-dextran complex ('Imferon', Benger). The estimation is quick and simple: it appears to be at least as accurate as the Evans-blue technique, and is subject to none of the disadvantages associated with Evans-blue.

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Addendum

Since this paper was prepared we have learned that the principle of using imferon as a means of estimating plasma-volume was tried by Scott, but after 3 cases the method was discontinued (J. M. Scott, *Brit. med. J.* 1956, ii, 635).

CHRONIC PROGRESSIVE POLYMYOSITIS AND SUBACUTE COMBINED DEGENERATION OF THE CORD

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IDIOPATHIC chronic progressive polymyositis together with skin changes and the gradual development of muscle contractures is uncommon. When this condition is associated with features of subacute combined degeneration of the cord, the diagnosis is more difficult, and the combination poses an interesting ætiological problem. The following case, which provides data suggesting a single disease complex rather than two coincidental diseases, may prove useful in the approach to other cases of polymyositis, dermatomyositis, and polyneuromyositis.

Case-report

In 1948 a married Englishwoman, aged 57, first noticed unsteadiness of the legs; she would fall over if lightly pushed. The legs gradually became weaker and she was unable fully to dorsiflex the feet. On attempting to walk without shoes she

fell backwards and for safe locomotion required a gradual increase in the height of her shoe-heels. At the age of 59 she was admitted to hospital and given intramuscular injections of a liver preparation. The weakness and imbalance of the legs became worse and caused readmission but no change of treatment, which was continued at weekly intervals. A fall resulted in fracture of the left tibia. She was developing what she described as " dropped feet " and was unable to rise easily from a sitting position.

At the age of 60 the hands began to feel numb and clumsy with some pins and needles. There was progressive weakness of both arms accompanied by a sensation of not being able to achieve a comfortable position of rest. An aching discomfort was felt in the arms and shoulders.

Examination, Investigations, and Treatment

Examination.—In November, 1952, when the patient was aged 61, she was found to have a sallow complexion with mild pallor. There was moderate generalised weakness of all four limbs. An abnormal fixed flexion deformity of both little fingers had been present all her life, and her mother had been similarly affected. The feet were described as high-arched. Knee-jerks were diminished; the right ankle-jerk was present and the left absent. There was some diminution of vibration and joint position senses at both ankles. The plantar responses were extensor. Muscular tonus was normal. The thigh muscles were somewhat wasted. The gait was unsteady without sensory ataxia. A little pitting ankle œdema was present.

Investigations in 1952 showed hæmoglobin 72% (10·7 g. per 100 ml.), colour-index 0·68, red blood-cells 5,330,000 per c.mm., white blood-cells 4300 per c.mm. (polymorphs 67%, lymphocytes 25·5%, large mononuclears 5%, eosinophils 2·5%); red cells showed some anisocytosis and poikilocytosis; no nucleated red cells in peripheral blood; platelets abundant. A histamine test-meal produced no free acid. Blood Wassermann reaction and Kahn test negative. Chest X-ray normal.

Treatment consisted of vitamin B_{12} 100 μg. daily, and tab. ferri sulph. gr. 9 t.d.s., which was later replaced by ferri et ammon. cit. gr. 30 t.d.s. A reticulocyte response of 2·4% from an original count of 0·6% developed in 4 days and subjective improvement followed. Vitamin-B_{12} therapy was continued at weekly intervals at home; and in September, 1953, the hæmoglobin was 104% and colour-index 0·98. On six occasions since 1952 the hæmoglobin level has not been less than 100%.

Course

Unfortunately the improvement was short-lived and the unsteady gait persisted. The paræsthesiæ in the hands were not relieved. In February, 1953, another heavy fall resulted in a fracture of the right tibia. In May, 1953, both ankle-jerks were absent; plantar responses unchanged. The position sense in the toes and vibration sense at the ankles were impaired.

In September, 1953, the patient became anxious and fearful, and lost confidence. A mild depressive state was diagnosed.

In March, 1954, typical tic douloureux began in the second division of the right trigeminal nerve, which required alcohol injection into the infraorbital nerve and eventually an infra-orbital-nerve avulsion and ganglion injection.

In June, 1956, observation of skin changes suggested a vitamin deficiency, but a pyruvate-tolerance test with glucose was quite normal. Ascorbic acid and a mixed vitamin-B preparation were given.

In November, 1956, an indolent skin lesion was seen on the left side of the forehead. It gradually extended with central scarring and was diagnosed as a basal-cell carcinoma.

At the age of 66, in September, 1957, the patient noticed difficulty in turning the forearms and an undue prominence of the flexor tendons in the forearms, which seemed to be " sticking out " near the wrist. The numb sensations once confined to the hands were now felt in the toes. There was no anæmia. Blood-pressure 150/90 mm. Hg. The arms and legs were abnormally thin. The skin of the arms and legs, especially over the shins and forearms, was thin and rather " tight " on the underlying tissues; it was somewhat bound down, and it

Fig. 1—Limited extension at the elbow; prominent contracted forearm tendons; patient attempting to extend the fingers; congenital deformity of little finger.

" crinkled " on movement; the underlying muscles, especially in the calves, thighs, and arms, felt hard though relaxed and not tender. The tendons of the biceps, the long flexors of the fingers (fig. 1) ham-strings, and achilles tendons were all very prominent owing to contractures of the muscles. The patient was unable to extend the fingers or elbows fully and the feet could not be dorsiflexed beyond about 80° (fig. 2). The extensor tendons of the toes were also prominent and the toes could not be completely plantar-flexed. The biceps, triceps, and supinator jerks were absent bilaterally. Knee- and ankle-jerks were all absent. The plantar responses were extensor, as in 1952. There was slight diminution in vibration and position senses in the lower limbs. The trapezius muscles and pectorals were wasted and very firm in consistence.

Further Investigations

Hæmoglobin 108% (16 g. per 100 ml.); colour-index 0·98; white blood-cells 4300 per c.mm. (differential count normal). Radiographs of chest and skull normal. Cervical spine X-rays revealed slight diminution of disc spaces c5–6, c6–7 with some osteophytic lipping. Radiographs of arm and leg muscles showed no calcification or ossification but only a diminished muscle mass. Barium studies on œsophagus, stomach, duodenum, and small gut were normal. Histamine test-meal confirmed the absence of free acid. Cerebrospinal fluid resting pressure 90 mm. H_2O; dynamics normal; clear colourless with a cell-count of less than 1 per c.mm; protein 25 mg. per 100 ml.; globulin (Pandy) no increase; Lange colloidal-gold curve and Wassermann reaction negative.

A four-day fat-balance test showed an average excretion of 3·1 g. total fat per day on a 100 g. intake. Serum proteins: albumin 2·9 g. per 100 ml., globulin 2·6 g. per 100 ml.; electrophoresis normal. Glucose-tolerance test: fasting blood-sugar 110 mg. per 100 ml.; maximum rise to 210 mg. per 100 ml. after $1^1/_2$ hours; no glucose appeared in the urine. The urine was albumin-free and contained in 24 hours 17-ketosteroids 4·5 mg. and 17-ketogenic steroids 6·3 mg. The erythrocyte-sedimentation rate was 12 mm. in the 1st hour (Wintrobe). The basal metabolic rate without sedation was normal.

A radioactive ^{58}Co vitamin B_{12} test (Berlyne et al. 1957) showed a 24-hour excretion of 0·6% of the dose. Retesting with a similar dose and 100 mg. of " intrinsic factor " pro-

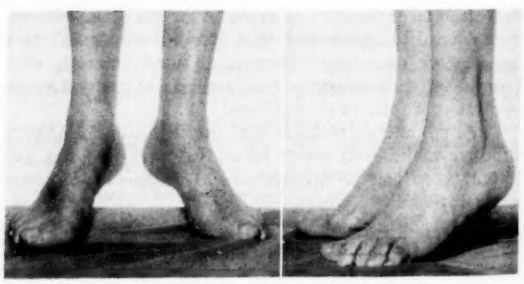

Fig. 2—Contractures of calf muscles; incomplete dorsiflexion of feet.

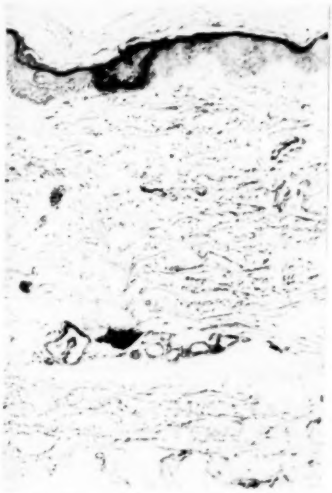

Fig. 3—Microscopic appearance of forearm skin (×80).

Fig. 4—Microscopic appearance of forearm muscle biopsy (×80).

duced an excretion of 3·5% of the dose in 24 hours—that is, a sixfold increase.

On electromyography the left rectus femoris felt woody to needle insertion, and the pattern was slightly gapped with a tendency towards increased short-duration potentials. There was no fibrillation. The result was consistent with myositis.

The forehead lesion was biopsied and showed solid branching trabeculæ of basal cells without obvious adnexal differentiation—basal-cell carcinoma.

Biopsy of skin and muscle of the left forearm where it was obviously abnormal showed the skin to have a thick, shreddy, horny layer (fig. 3); one or two arterioles in the dermis showed mild lymphocytic cuffing. The muscle showed focal chronic inflammation (fig. 4), the cells being mainly lymphocytes, though some large mononuclears were also present. The muscle bundles were normally striated. There was no increase in sarcolemmal nuclei and no degenerative change. The bundles were uniform in size. Pathological diagnosis: chronic dermatitis and myositis.

Treatment and Progress

Prednisone 5 mg. four times a day was given in January, 1958. The patient felt improved, though no objective change was apparent. Intramuscular vitamin B_{12} 100 μg. weekly was maintained. High-heeled boots were fitted to give more stability for walking. In May, 1958, after continuous prednisone therapy, no improvement had occurred. Walking without boots was as difficult as ever. No change in skin, muscle contractures or consistence, nor in reflexes was observed.

Discussion

When this patient first attended with anæmia, paræsthesiæ, and difficulty in walking, diminished ankle-jerks, sensory defect, and achlorhydria, the most likely diagnosis appeared to be subacute combined degeneration of the cord, although the reticulocyte response can be ascribed to iron as previous long-continued vitamin-B_{12} therapy had not abolished the anæmia which was of iron-deficiency type. The iron deficiency might, however, have been " exposed " by the vitamin-B_{12} therapy in a mixed deficiency. It was thought that the " high arches " were developmental.

As the next eight years passed, although the patient was given vitamin-B_{12} weekly, the symptoms never improved. Progressive muscle contracture developed gradually with global weakness and loss of tendon reflexes. Paræsthesiæ were unrelieved. Tic douloureaux and mental depression might have been purely coincidental. The basal-cell carcinoma might have been connected with chronic dermatitis, and less probably with the " dermatomyositis " syndrome. There were no generalised signs of inflammation or infection.

The features indicating subacute combined degeneration were paræsthesiæ, sensory defects in the feet, loss of ankle-jerks, and extensor plantar responses. Further evidence was achlorhydria and an abnormally low absorption of vitamin-B_{12}, increased six times by intrinsic factor.

The features of a myositis were muscle weakness and atrophy, gradually progressive muscle contractures, hard " woody " muscles, loss of tendon reflexes pari passu with muscle involvement, and confirmation by microscopic examination of muscle, texture to needle insertion, and electromyography.

Polymyositis may take any of many different forms (Garcin et al. 1955).

The polyneuromyositis described by Senator (1888) with loss of reflexes, sensory loss, and paræsthesiæ is reminiscent of our case. Gowers (1899) believed that the peripheral nerves could be involved. Myositis ossificans is easily distinguished by radiographs. A pseudomyopathic type of polymyositis described by Furtado and Alvim (1945) involved ocular muscles with a myositic histological picture. The so-called pseudomyasthenic polymyositis causes dysphagia and ocular pareses, and it may respond to neostigmine. There is a senile chronic myosclerosis. Poikilodermatomyositis, described by Petges and Clejat (1906), included atrophic sclerosis of the skin with mottled pigmentation, telangiectases, and partial alopecia rather like a radiation dermatitis; it was similar to the poikilodernia atrophicans vasculari of Jacobi (1908) except for the myositis. Sheard (1951) had the impression that such cases were really dermatomyositis of gradual onset with a chronic course.

The present case apparently resembles chronic progressive myositis fibrosa. Adams et al. (1953) described this as an insidious peripheral-muscle atrophy with contractures, weakness, malaise, and easy fatiguability. It is usually painless. Eventually the laryngeal, pharyngeal, and respiratory muscles may be involved. It tends to affect adults, but it progresses over weeks rather than years as in our patient. Blau (1938), who reported two cases, said that skin lesions were unusual. The patient, aged 11, described by Stuart and McGregor (1951) had histological features of progressive muscular dystrophy without round-cell infiltration of muscle. Strong's (1949) case was remarkably like ours; but six cases of Christenson and Levison (1950) were quite unlike ours. Matthews and Burn (1953), who described three cases of chronic polymyositis, declared that " the condition of generalised myositis fibrosa is probably not a distinct entity ".

Garcin et al. (1955) describe *myosites fibreuses généralisées progressives* as an insidious process with stiffening of the limbs and hardness of muscles beginning as a small hard zone.

Cases which begin with localised induration are classified by Burton et al. (1923, 1931) as " myositis fibrosa, the localised form " and may represent a different disease from the symmetrical generalised type. Nattrass (1955) and Walton (1955) describe polymyositis in adults with symmetrical wasting of scapular and upper arm muscles and weakness of spinal and pelvic muscles. Transient improvement was produced by cortisone. Nattrass suggests that polymyositis in later life either

resembles a chronic muscular dystrophy with or without slow deterioration or is associated with dermatitis and a more severe acute illness. Walton (1955) emphasises the resemblance of most cases of polymyositis to other " collagen " diseases.

The menopausal muscular dystrophy of Shy and McEachern (1951) should be considered in diagnosis. There is progressive girdle weakness; the muscles are soft and show necrosis, loss of striations, proliferation of sarcolemmal nuclei, and fibre phagocytosis.

In Nevin's (1936) two cases of muscular degeneration in late adult life the proximal muscles were affected and there was no contracture. The muscle changes resembled a dystrophic process.

Stuart and McGregor (1951) suggested that myositis fibrosa generalisata was a dystrophy, because of the increase in sarcolemmal nuclei, fatty infiltration, and variability in fibre size. Our case was unlike this type: only atrophy, induration, and round-cell collection were seen—a disorder termed " polymyositis interstitialis chromica fibrosa " by Benedik et al. (1944).

Adams et al. (1953) say that in the more chronic cases of polymyositis the skin is brownish, tight, shiny, and atrophic—which is similar to that in our case. Garcin et al (1955) suggest that the skin is intact. Burton et al. (1923) observed a case for 10 years and noted that after this time the skin had become smooth and thin.

No record of association of subacute combined degeneration with chronic progressive polymyositis has been found by us, nor any reference to defective vitamin-B_{12} absorption in the latter condition. At first sight the two may seem coincidental. Supposing that defective B_{12} absorption were the primary lesion, then one might consider whether myositis could be due to this. It would be hard to conceive why vitamin B_{12} did not stop the myositic process in the present case.

It is much easier to visualise a generalised tissue disturbance including myositis, skin change and gastro-intestinal mucosal changes leading to defective B_{12} absorption. No additional evidence from the fat-balance test, glucose-tolerance curve, or barium studies was forthcoming. We do not know how long the patient had had muscle involvement before she was first seen, but contractures of the calf muscles were already evident. Spread of myositis has been slow but steady. There was no chronological separation of the features of subacute combined degeneration of the cord from those of myositis. This strongly suggests a single process. It is interesting that vitamin-B_{12} therapy did not prevent or arrest the extension of paræsthesiæ. This suggests a " neuromyositis " of peripheral type unassociated with vitamin-B_{12} deficiency. The features of subacute combined degenerative of the cord hardly changed at all in 8 years. We assume that vitamin-B_{12} therapy arrested this part of the disease but had no effect on the myositis. Also curious are the " complications ". The skin cancer, trigeminal neuralgia, and mental depression might also be part of the generalised tissue disease. Perhaps most patients with chronic polymyositis do not live long enough for malabsorption to become evident.

Scleroderma, which may be associated with gastro-intestinal changes and absorption defects, may be linked with the present type of case on the basis of collagen disease. There was, however, only a fleeting resemblance to scleroderma in the skin changes.

Summary

Chronic progressive myositis with muscle contractures was associated with chronic atrophic dermatitis, in a woman aged 66.

There were clinical features of subacute combined degeneration of the cord and defective vitamin-B_{12} absorption. The patient also had basal-cell carcinoma of the scalp, mental depression, and trigeminal neuralgia.

A widespread mucocutaneous neuromuscular disturbance may account for the whole syndrome as a single collagen-disease process.

We thank Prof. A. C. P. Campbell and Dr. Raymond Whitehead for the pathological report, Dr. M. Q. Birkbeck for the electromyography, and Dr. Robert Ollerenshaw for the photographs.

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CEREBRAL REGULATION OF SODIUM EXCRETION

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We have studied the nervous regulation of sodium excretion by crossed-circulation experiments in dogs. The head of one animal was isolated from its trunk except for the nervous connections, and perfused with blood from another animal. Using this preparation we have shown previously (Földi, Kovách, Róheim, Papp, Koltay 1957) that the intracarotid injection of hyperosmotic sodium-chloride solutions into the humorally isolated head produces a reflex increase of renal excretion of sodium. This increase is independent of antidiuretic-hormone (A.D.H.) action; for, although the intracarotid injections stimulate the secretion of A.D.H. (Verney 1947), the isolation of the head prevents the A.D.H. from entering the circulation of the trunk. There is also no increase in the level of sodium in the plasma from the trunk to account for the increase in renal excretion of sodium.

We have now compared the effect of intracarotid injections of other hyperosmotic solutions on the excretion of sodium, and have attempted to assess the roles of the carotid sinuses, the renal nerves, and the adrenals in the production of sodium diuresis.

Procedure

Dogs of each sex were anæsthetised with chloralose in a dose of 0·1 g. per kg. body-weight. The vertebral arteries and veins, the cervical lymphatic trunk, and the internal jugular and spinal veins were ligated, and the remaining vascular connections in the skin and muscles were clamped. The head was perfused from a donor dog through the carotid arteries

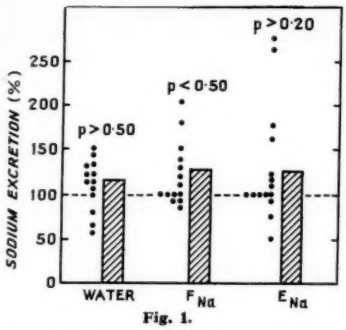

Fig. 1.

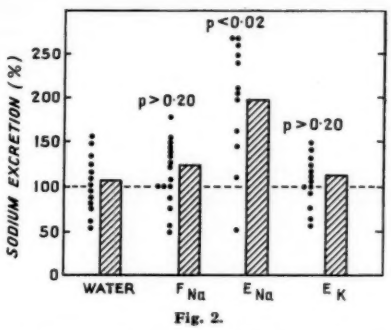

Fig. 2.

Fig. 1—The effect of intracarotid injection of hyperosmotic mannitol solution in crossed-circulation experiments.

In all the figures, ordinate = sodium excretion as a percentage of the control value (100%). Each dot represents one experiment. The columns represent the mean. W = water excretion, F_{Na} = sodium filtration, E_{Na} = sodium excretion, E_K = potassium excretion. P values are the results of the statistical analysis.

Fig. 2—The effect of intracarotid injection of hyperosmotic sodium-phosphate buffer in crossed-circulation experiments.

and external jugular veins. Heparin was used as an anticoagulant. After the operation the only connections between the head and the trunk of the acceptor animal were through the spinal cord and the vagus and sympathetic nerves.

Our preparation gave a sufficient degree of humoral isolation of the head from the trunk. This was proved by the fact that about an hour after the crossed circulation had been established water excretion in the acceptor animal usually increased. During this time the A.D.H. already circulating in the trunk had been destroyed or excreted, and the lack of A.D.H. then caused a polyuria. On the other hand there was no rise of the serum-sodium level in the trunk when the sodium level was increased in the cerebral circulation. The only humoral connection left between the head and trunk was in the substance of the spinal cord. Blood-flow through this region depends largely on the blood-pressure gradient between donor and acceptor. If the blood-pressure in the two animals is equal, the amount of blood flowing into the trunk is between 0·5 and 1·0% of the cerebral blood-flow; after dissection of the neck distal to the anastomosis this value may reach a maximum of 5%. Details of the operative techniques and of the degree of isolation of the head have been given previously (Kovách 1954, Kovách et al. 1957).

In the denervation experiments both carotid sinuses were denervated immediately before the injection of sodium chloride. The effectiveness of the denervation was judged by the rise of arterial blood-pressure afterwards. The left kidney was denervated by cutting the lower thoracic and upper lumbar part of the left sympathetic chain, and the splanchnic nerves, through a thoracic incision. This operation was done a week before the actual experiment. Adrenalectomy was performed in two stages; the adrenalectomised animals were maintained with cortisone, 25 mg. daily.

Results

Effect of Hypertonic Solutions other than Saline

Fig. 1 shows the effect of injecting mannitol (15 ml. of 30% solution) into the carotid artery of the acceptor dogs. The excretion of sodium increased to 135% of the control values (mean of 10 experiments). This difference was not significant ($P > 0.05$).

Fig. 2 shows the effect of injecting a sodium-phosphate-buffer solution (5·4% pH 7·3). The sodium excretion increased to 196% of the control values (mean of 11 experiments), which was significant ($P < 0.02$). Water excretion, sodium-filtration rate, and potassium excretion did not change.

Effect of Denervating the Carotid Sinuses and One Kidney

The intracarotid injection of hypertonic sodium-chloride solution raised the excretion of sodium in the innervated kidney to 262% and in the denervated kidney to 249% of the control values (means of 17 experiments, fig. 3). These increases were significant ($P < 0.02$). Water excretion also rose significantly; the sodium-filtration rate and potassium excretion were unchanged.

Effect of Adrenalectomy

The experiments, 6 in all, were done a week after the removal of the second adrenal. The intracarotid injection of hypertonic sodium-chloride solution did not increase the excretion of sodium in the adrenalectomised animals.

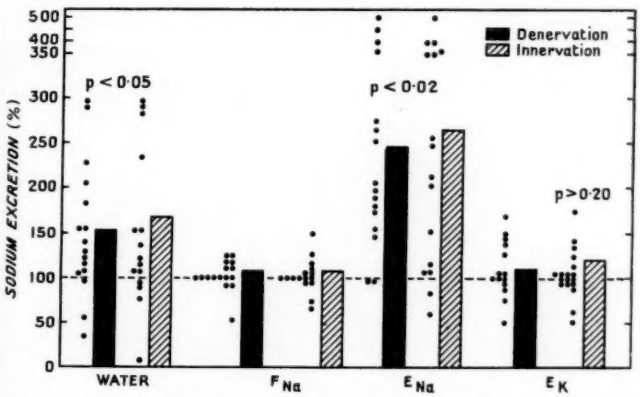

Fig. 3—The effect of intracarotid injection of hyperosmotic sodium-chloride solution in crossed-circulation experiments after denervation of the carotid sinuses and one kidney.

Conclusions

We conclude that the increase in sodium excretion after the intracarotid injection of hypertonic sodium solutions is the result of a discharge of neural impulses which act through the adrenals.

The sodium/potassium ratio in the urine rose after the intracarotid injection of sodium chloride, suggesting that the secretion of adrenal mineralocorticoid hormones decreased.

A question to be decided by further experiments is whether A.D.H., liberated through the intracarotid injection of a hyperosmotic solution, may act on some part of the central nervous system, thus stimulating sodium excretion through nervous impulses. Other humoral agents may also have to be considered.

Summary

In dogs the intracarotid injection of a hyperosmotic sodium-chloride solution into the "humorally isolated" head increased the renal excretion of sodium through a central nervous mechanism.

The same effect was produced by the intracarotid injection of a hyperosmotic sodium-phosphate solution, but a hyperosmotic solution of mannitol had no significant effect on the renal excretion of sodium.

Denervation of the carotid sinuses with denervation of one kidney by unilateral sympathectomy did not prevent the increase in sodium excretion after the intracarotid injection of a hypertonic solution of sodium chloride.

The response could not be reproduced in adrenalectomised animals maintained with cortisone.

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HÆMOLYSIS CAUSED BY TUBING IN EXTRACORPOREAL CIRCULATION

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HÆMOLYSIS in a pump-oxygenator circuit, designed for experiments on extracorporeal circulation in dogs, prompted us to investigate the effect of the tubing on the blood.

An experiment was performed as follows:

Samples of new tubing made from red rubber,[1] translucent rubber,[2] siliconed rubber,[3] crystal-grade polyvinyl chloride (PVC),[4] polyvinyl chloride,[5] and beverage hose,[6] having the same internal diameter (6 mm.), were cut into equal lengths (45 cm.). The tubes were used as supplied by the manufacturers.

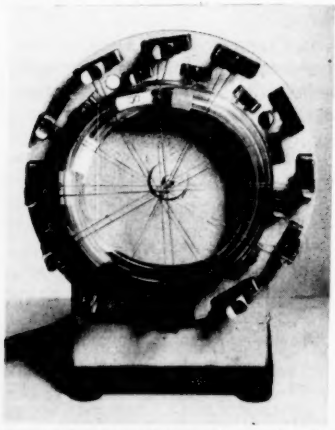

Fig. 1—Experimental circuits fixed to the vertical disc before rotation.

Each tube was a quarter filled with blood (3 ml.) containing heparin (5 units per ml. blood) as an anticoagulant. In all experiments the blood was freshly drawn from the same human donor. The ends of each tube were joined together as accurately as possible, using an external connector. Thus a closed circuit for the blood was formed in each tube.

The circuits were then placed on a vertical disc (fig. 1) and turned in their long axes at 17·5 r.p.m. for an hour. By this method a continuous flow at constant velocity was produced through the circuits by gravity, and the effects of using a pump were avoided. The velocity of flow was 7·8 m. per minute, which is equivalent to a flow-rate of 222·5 ml. per minute.

At the end of an hour the blood in each circuit was analysed for plasma-hæmoglobin. As a control, the same quantity of heparinised blood (3 ml.) was left standing in a 3 × 0·5 in. glass tube.

This experiment showed hæmolysis of different degree in the circuits:

Circuit tubing	*Plasma-Hb* (mg. per 100 ml.)
Red rubber	137
Translucent rubber	162
Siliconed rubber	137
Crystal-grade PVC	200
PVC	62
Beverage hose	20
Control	0

Having obtained these results, we repeated the experiment but this time the tubes were washed through with tap water, distilled water, and normal saline before the blood was added. The results were:

Circuit tubing	*Plasma-Hb* (mg. per 100 ml.)
Red rubber	135
Translucent rubber	132
Siliconed rubber	145
Crystal-grade PVC	162
PVC	390
Beverage hose	17
Control	0

The effect of storing the blood before use was then tested. Blood was drawn and heparinised as before, then kept in a refrigerator for 12 hours before the experiment was repeated. The results were:

Circuit tubing	*Plasma-Hb* (mg. per 100 ml.)
Red rubber	730
Translucent rubber	1010
Crystal-grade PVC	730
PVC	145
Beverage hose	42
Control	0

The naked-eye appearance of hæmolysis of this extent is shown in fig. 2.

When the above experiments, which were performed at room temperature, were repeated at 37°C in a thermostatically controlled room the results were unchanged.

Specimens of 'Tygon' tubing (S-22-1) tested later produced hæmolysis of the same order as the beverage hose.

Having found that tubing can by itself produce hæmolysis and that the extent of hæmolysis varies with the material from which the tube is made, we attempted to find the cause of the hæmolysis. Beverage hose was used, because it was the least destructive, and by varying the

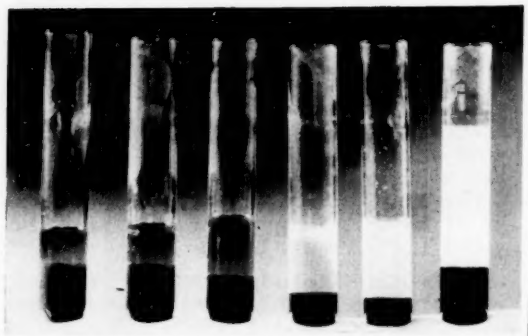

Fig. 2—Hæmolysis produced experimentally in stored blood.
The samples (left to right) are from circuits made from red rubber, translucent rubber, crystal-grade PVC, PVC, and beverage hose, and from a control.

The tubing was made by:
1 & 2. J. Franklin Ltd., 15, Colveston Crescent, London, E.8.
3. Esco Rubber Co., 2, Stothard Place, London, E.C.2.
4 & 5. Portland Plastics Ltd., Bassett House, Hythe, Kent.
6. B.X. Plastics Ltd., Miltoid Sales, 34, Royal College Street, London, N.W.1.

technique of the experiment slightly in each case, the following factors were investigated:

(1) If there was a hæmolytic agent in the tubing, by doubling the amount of blood (6 ml.) in one circuit there should be less hæmolysis than in a standard circuit (3 ml.). We found that the hæmolysis in the circuit with 6 ml. of blood was greater (100 mg.) than in the standard circuit (60 mg.). The reason may be that more of the blood in the fuller tube is circulating, and at any particular moment there is less blood stationary on the walls of the tubing.

(2) We then tested the effect of the connection. Four connections were made in one circuit, and the result compared with that from a standard circuit with one connection. There was an increase of 5% per connection in the circuit with four connections (124 mg.) over that with one connection (109 mg.).

(3) We found that by halving the velocity of flow through the circuits (to 3·9 m. per minute) hæmolysis was abolished. At the previous speed (7·8 m. per minute) there had been hæmolysis (62·5 mg.), and at double this speed (15·6 m. per minute) the hæmolysis had greatly increased (180 mg.).

(4) The duration of flow had no effect on hæmolysis as long as the velocity was kept low.

(5) By doubling the internal diameter of the tubing the velocity of flow could be doubled and the rate of flow increased eight times without the amount of hæmolysis being increased.

(6) Varying the strength of heparin had the following effect on the hæmolysis:

Heparin (units per ml. blood)	*Plasma-Hb* (mg. per 100 ml.)
2·5	16
5	14
10	10
20	4

(7) The effect of different anticoagulants was then tested, and it was found that acid/citrate/dextrose produced significantly less hæmolysis than heparin, heparin/dextrose, or edetic acid ('Versene'). As acid/citrate/dextrose dilutes the blood more than the other anticoagulants, we studied the effect of diluting heparinised blood to the same extent (1 in 6) with different diluents, thus:

Anticoagulant and diluent	*Plasma-Hb* (mg. per 100 ml.)
Heparin + Ringer's solution	66
Heparin + own plasma	48
Heparin + dextran	250
Acid/citrate/dextrose	66
Heparin undiluted	72

The results of our experiments so far had shown how hæmolysis may be diminished, but had not shown its cause. It seemed possible that hæmolysis was due to direct trauma to the red cells by the internal wall of the tubing. Macroscopic examinations and microscopic appearances of the walls showed that irregularities did exist. We therefore submitted samples of all types of tubing to Messrs. Taylor, Taylor, & Hobson for examination on a 'Talysurf' instrument.

The method involved passing a diamond stylus along the inside of the tube in a direction parallel to its long axis, and bearing on the tubing with a force of 100 mg. The stylus was shaped as a 90° cone with a tip radius of 0·0001 in. The roughness of the surface created a vertical movement of the stylus which was amplified electrically and recorded as a graph. The horizontal movement, obtained by a gearbox mechanism, drew the stylus at 1/100th of the paper-recorder speed. There was therefore a distortion in the graphs due to lengthwise compression. In the graphs shown (fig. 3), the horizontal magnification is 100 in each case; the vertical magnification is 2000 in the rougher tubes but is increased to 10,000 in the smoother tubes to exaggerate slight irregularities in the surface.

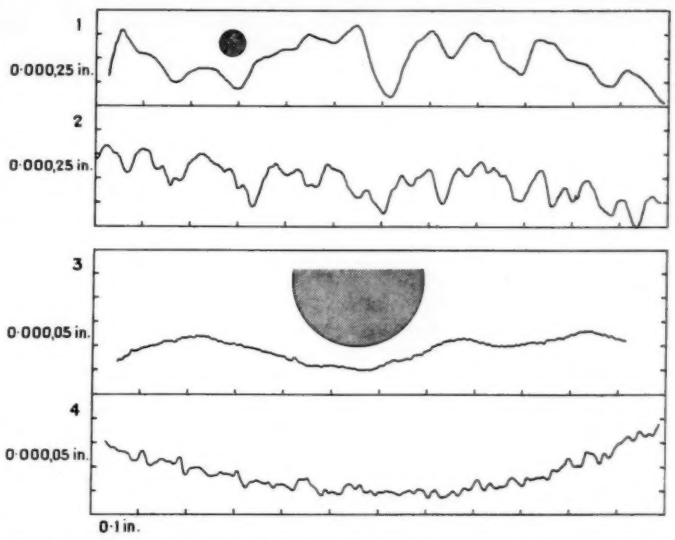

Fig. 3—Graphs recorded from the inner walls of tubing made from (1) red rubber, (2) translucent rubber, (3) beverage hose, and (4) tygon (S-22-1).

The horizontal magnification in each graph is 100; the vertical magnification is 2000 in (1) and (2), and 10,000 in (3) and (4).

The circles in (1) and (3) represent the relative size of a red blood-cell on the vertical scale.

Three sections of each tube were tested in this way, and from the graphs the tubes could be classified in order from smoothest to roughest:

Tubing	*Test section* A	B	C
Red rubber	7th	7th	7th
Translucent rubber	6th	5th	6th
Siliconed rubber	3rd	3rd	4th
Crystal-grade PVC	4th	4th	3rd
PVC	5th	6th	5th
Beverage hose	1st	1st	1st
Tygon (S-22-1)	2nd	2nd	2nd

Summary and Conclusions

The destructive effect on circulating blood of tubing of different materials were compared experimentally.

The experimental conditions are thought to be more severe than would be met during extracorporeal circulation of the same duration, since all the blood was circulating continuously and had no respite in reservoirs or in the body.

The results showed that:

(1) Blood flowing through tubing was destroyed to an extent which varied with the material from which the tubing was made.

(2) Washing the tubing through before use did not materially alter this effect.

(3) Storage of heparinised blood before use appeared to increase the liability to destruction.

(4) Temperature, within the range tested (20–37°C), had no effect.

(5) For any given tube, there appeared to be a critical velocity of flow, which, if exceeded, produced hæmolysis.

(6) High rates of flow can be obtained with tubing of wide internal diameter and low destructibility.

(7) Dilution of the blood with physiological solutions decreased the liability to destruction.

In general, the smoother the internal wall of the tube, the less hæmolysis was produced.

The conclusion from these experiments is that, of the materials tested, only beverage hose and 'Tygon' (S-22-1) tubing are suitable for use in a pump-oxygenator at the rates of flow desired.

The recommended internal diameters of these tubes are:

6 mm. for flow-rates up to 110 ml. per minute.
12 mm. for flow-rates up to 900 ml. per minute.
24 mm. for flow-rates up to 7 litres per minute.

Within the limits of extracorporeal circulation these diameters allow flow without hæmolysis indefinitely.

We wish to thank Messrs. Taylor, Taylor, & Hobson, of Stoughton Street, Leicester (a division of Rank Precision Industries) for the 'Talysurf' recordings.

SPONTANEOUS NECROSIS IN PITUITARY TUMOURS
(PITUITARY APOPLEXY)

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IT is not always realised how wide the repertory of presenting symptoms with pituitary tumours can be. It ranges from the classical mode, with temporal-field loss, and signs of acromegaly, or pituitary insufficiency, through various symptoms resulting from extrasellar extension to remote endocrine effects such as hypothyroidism or adrenal dysfunction. Or the first sign may be the dramatic events which mark sudden tumour infarction—the syndrome of "pituitary apoplexy". This presentation is perhaps the least known—not surprisingly, for it is relatively rare. (It was not seen in any of the 117 consecutive cases of pituitary tumour analysed in 1953 by Nurnberger and Korey.) Nevertheless, it is not so uncommon that the general physician can afford to neglect it. Chance has lately offered us two examples.

Case-reports

THE FIRST PATIENT

A foreman moulder, aged 64, was admitted to the Queen Elizabeth Hospital (no. 438596) on Jan. 30, 1958. Three weeks earlier, in the course of an evening, he had developed severe pain behind and above the left eye. This spread to the root of the nose and it was intense enough to interfere with sleep. By morning it had gone, but he was now unable to open his left eye; and, on lifting the upper eyelid, he saw double. His left eye was immovably deviated to the outer canthus. Ptosis and ocular palsy persisted, but the headache disappeared and he felt well generally.

He had been deaf in his left ear since a radical mastoidectomy in 1938. In 1955 a perforated gastric ulcer had been sutured. Puberty had been late, with onset at the age of 20; and he did not start to shave until he was 24, never needing to do so more than once a week. Nevertheless, sexual function and libido had always been normal, and he had three children.

Examination and Investigations

He had a left third-nerve palsy, with ptosis, external rotation of the eye, and loss of pupillary reflexes. The pupil was only slightly dilated. The fourth nerve was also paralysed. The corneal reflex was active, and there was no trigeminal cutaneous sensory blunting. The visual fields were full on perimetry and screening, and acuity was normal. There was no cranial or carotid bruit, nor signs of meningism. His facial appearance hinted at acromegaly, the pubic and axillary hair was somewhat deficient, but the genitalia were normal. The blood-pressure was 160/90 mm. Hg.

Skull X-rays showed destruction of the pituitary fossa with undermining of the anterior clinoids, thinning of the posterior clinoids, and extensive erosion of the sellar floor. Sagittal tomographs and left carotid angiography supported the diagnosis of a primary pituitary neoplasm. The electroencephalogram and the chest radiographs were normal. Hæmoglobin was 10·7 g. per 100 ml., the white-cell count 5000 per c.mm., and the erythrocyte-sedimentation rate 14 mm. in one hour (Wintrobe). The Wassermann and Kahn reactions were negative, and the basal metabolic rate was −3% (Aub du Bois). The urinary 17-ketogenic steroid excretion was 18 mg. and the urinary gonadotrophin output 5 mouse-units per 24 hours. Serum-sodium was 126 mEq., serum-potassium 4·1 mEq., and serum-chloride 102 mEq. per litre; serum-cholesterol 202 mg. per 100 ml., serum-proteins 6·0 g. (albumin 3·5 g., globulin 2·5 g.), serum-urea 33 mg., serum-alkaline-phosphatase 12·3 units (Jenner and Kay), and acid-phosphatase 4·0 units. The fæces contained no occult blood.

Operation and Progress

On Feb. 19, 1958, Prof. Brodie Hughes explored the pituitary region by a left frontal route. There was no displacement of the optic nerves, chiasma, left internal carotid artery, or cavernous sinus. The diaphragma sellæ was not bulging or tense, but on incision thick yellowish fluid was encountered. This was aspirated, 25 ml. being obtained. Inspection of the sella then showed a clean smooth cavity with no sign of tumour or pituitary tissue. Culture of the aspirate was sterile, and microscopy showed amorphous necrotic material with many fat-laden cells, mostly degenerate, and only a few polymorphs.

After operation, penicillin and cortisone were given. Spontaneous recovery of the paralysed ocular muscles had already begun before operation, and it was well advanced by the time of the patient's discharge from hospital on March 2. By June his ophthalmoplegia had completely resolved and he was very well. Because his blood-pressure had risen from 135/70 to 200/105 mm. Hg on cortisone, 25 mg. twice daily, this maintenance dose was halved.

Précis.—A man aged 64 developed left fronto-orbital headache, quickly followed by left third and fourth nerve palsy, with an abruptness suggesting intracranial carotid aneurysm. Skull X-rays showed gross sellar enlargement, pointing to pituitary tumour, with presumed extrasellar extension. At operation complete liquefactive necrosis of the sellar contents was found, the material being sterile on culture, and histologically non-purulent. Final diagnosis of spontaneous tumour destruction from infarction was made. Recovery was uneventful.

THE SECOND PATIENT

A married woman was admitted to the Queen Elizabeth Hospital aged 47 (no. 439730) on March 31, 1958. She had been well until two months earlier when she began to suffer from vertical headaches. These became persistent, disturbing her at night: they were aggravated in the daytime by jarring or physical effort. Also she started to vomit after meals. She did not consult her doctor until March 29, when she woke with a violent pain in her head and found that she could not see.

When she was admitted to another hospital her temperature was 103°F, and she had neck rigidity and a positive Kernig sign. She was blind, with dilated and unreactive pupils, but with no other neurological signs. Her pubic and axillary hair were extremely sparse and her skin was generally hairless, pale, and thin. Her blood-pressure was 90 mm. Hg systolic, diastolic reading uncertain. The cerebrospinal fluid pressure was raised (210 mm. water) and the fluid was turbid with many polymorphs. Proteins 200 mg. per 100 ml., sugar 67 mg., and sodium chloride 650 mg. Culture sterile.

On treatment with penicillin, 1 million units daily, and sulphadiazine, 1·5 g. four-hourly, her temperature fell; but on March 31 she became semiconscious. Her pupils were now small, but they still failed to react to light. Her whole right side was weak, and she had a right extensor plantar response. Her blood-pressure was 130/80.

She was transferred under our care that evening. Her husband told us that they had had two children (now 22 and 20) and that she had suffered from menorrhagia from the birth of the second until her menopause at 43. She had never had much pubic or axillary hair, her complexion had always been pale, and for many years she had been intolerant of cold.

Examination and Investigations

She could be temporarily roused, but her speech was unintelligible. Her pupillary diameter fluctuated slightly. The optic discs were normal. She had severe right hemiparesis without definite sensory loss. Her pronounced neck stiffness with only slightly restricted straight-leg raising pointed to predominantly basal meningeal irritation. She looked dehydrated and her pulse was rapid and feeble. Her blood-pressure was 95/60 and her temperature 98°F. Skull radiographs showed considerable enlargement of the pituitary fossa. The white-cell count was 11,000 per c.mm. (polymorphs 92%, lymphocytes 6%, monocytes 2%); hæmoglobin 10·8 g. per 100 ml.; erythrocyte sedimentation-rate 56 mm. in one hour (Wintrobe). Serum-urea was 28 mg. per 100 ml. Serum-sodium was 117 mEq. per litre, serum-potassium 5·1 mEq. and serum-chloride 89 mEq.

Initial Treatment

Penicillin 500,000 units three-hourly, streptomycin, 1 g. twice daily, prednisone 10 mg. six-hourly, sodium thyroxine, 0·1 mg. twice daily, were given. High-protein fluids with added salt were administered by intragastric drip. Her level of consciousness, the dysphasia, the right hemiparesis, and the neck stiffness, gradually improved; and the blood-pressure settled around 110/80 mm. Hg.

Operation and Progress

On April 8, Mr. E. A. Turner exposed the pituitary fossa through a right frontal approach. Brain tension was not high, but the cerebral vessels were congested and the subarachnoid fluid of the sulci was milky. A large pituitary tumour was found, pushing up the chiasma and optic nerves which were otherwise normal. The sellar diaphragm was not tense. Through a needle a small quantity of necrotic material was aspirated from the interior of the tumour, and the contents of the sella were then removed by scoop and by suction. At the end of operation only a small portion of tumour remained: this was adherent to the hypothalamus. Most of the material removed was amorphous and necrotic: occasional tissue fragments indicated a chromophobe adenoma.

After a few days full consciousness was regained. Her speech was normal, but it was apparent that her memory was very faulty. She could still not see and she had a trace of hemiparesis. Her dehydration and electrolyte imbalance were slow to resolve; but by May 6 serum-sodium was 135 mEq. per litre, serum-potassium 3·6 mEq., and serum-chloride 104 mEq. At this stage her fasting blood-sugar was 74 mg. per 100 ml. and her serum-cholesterol 195 mg. The electrocardiogram and electroencephalogram were both normal.

The patient was sent home on June 28, 1958. She did not recover her sight, and she now has optic atrophy. Right-sided weakness is still just detectable; and, though her intellectual vigour has steadily improved, her memory is still poor. Maintenance therapy has been slowly reduced to cortisone 25 mg. daily, and sodium thyroxine, 0·1 mg. three times a day.

Précis.—A woman of 47, after two months of recurrent vertical headaches, abruptly went blind with severe general head pain. She was found to have meningitis with fever; and right hemiplegia followed. There were signs of pituitary hypofunction with a radiologically enlarged sella, and hypoadrenalism. It was thought that intracranial infection had developed, secondary to invasion of the sphenoidal sinus by a pituitary tumour, but the cerebrospinal fluid was sterile. At operation an extensively necrotic chromophobe adenoma was found, diagnosed as the result of spontaneous infarction. There was no recovery of sight afterwards, and memory remained impaired for many weeks.

Discussion

Minor degenerative changes—such as small cysts or areas of hæmorrhage—are a relatively familiar feature of hypophysial adenomata (Kraus 1926). Extensive and acute destruction is less well known, although isolated cases have been described. It may occur spontaneously (Bleibtreu 1905, Benjamin 1929, Dingley 1932, Aitken and Russell 1934, Voss 1938, Coxon 1943, Kirshbaum and Chapman 1948), after head injury (van Wagenen 1932), or after irradiation (Dott et al. 1925, Kux 1931, Sosman 1939). Since 1950, when Brougham et al. published 5 additional cases, more attention has been directed to it (Fountain et al. 1951, List et al. 1952, Schnitker and Lehnert 1952, Röttgen and Peters 1952, Müller and Pia 1953, Philippidès et al. 1956). Uihlein et al. (1957) stated that 71 cases were on record.

Massive sudden degeneration is generally thought to have a vascular cause: the usual finding is hæmorrhagic necrosis of the pituitary body, in which sometimes the necrosis and sometimes the hæmorrhage predominates. Entirely non-hæmorrhagic necrosis was reported by Philippidès et al. (1956), though others may belong to this group (Monro 1913, Long 1927). The weight of present opinion attributes infarction to circulatory embarrassment in the sella, caused by a rise in pressure from the tumour growing in a confined space (Brougham et al. 1950, List et al. 1952, Uihlein et al. 1957). Alternatively, a primary abnormality may make the adenomatous blood-vessels unduly susceptible to rupture or occlusion (Müller and Pia 1953), or the tumour may simply outgrow its blood-supply (Brougham et al. 1950). It is also possible that the peculiarities of the hypophysial circulation itself are important. According to Xuereb et al. (1954 a, b) the glandular sinusoids receive blood only by way of a portal system which arises in the pituitary stalk from an intricately patterned capillary bed. This is fed by the hypophysial arteries which anastomose freely with each other. The complexity of the vascular arrangements may reflect an equally complex mechanism regulating pituitary blood-flow, and the growth of an adenoma may interfere with the delicacy of its adjustment. A comparable dynamic explanation has already been postulated for postpartum pituitary necrosis (Xuereb et al. 1954a, Daniel and Prichard 1958); and indeed there is good evidence that interference with stalk circulation can cause necrosis, both in man (Russell 1956, Daniel et al. 1958) and in animals (Daniel and Prichard 1956, 1957).

Pituitary apoplexy commonly presents against an essentially symptomless background. Abrupt headache signals its onset; and this may be followed by loss of sight, diplopia, drowsiness and confusion, or coma. There may be signs of meningeal irritation, with blood or pus in the cerebrospinal fluid, and of circulatory collapse. All these features can be accounted for readily. Acute swelling of the pituitary mass at or just after infarction may exert pressure dorsally on the chiasma or laterally on structures in the cavernous sinus. If the sellar diaphragm is torn, blood can escape into the subarachnoid space, or necrotic matter may be extruded which excites white-cell pleo-

cytosis. Headache may be due to raised intrasellar tension, meningeal reaction, or both; and profound circulatory collapse and electrolyte shift are features of acute addisonian crisis precipitated by removal of anterior-pituitary control. Lastly, compression of the hypothalamus may be a contributory cause of death—a common outcome.

Both our cases had a white infarction. In the second patient necrosis was extensive but not complete: in the first patient it had progressed to total liquefaction of all pituitary tissue, which has not been previously described. Both on clinical grounds and on the laboratory findings we regard this liquefaction as sterile necrosis, not as an abscess (Whalley 1952, Hamman 1956).

The third-nerve and fourth-nerve paralyses in the first patient and the abrupt and permanent blindness in the second must be attributed to sudden stretching or compression of the nerves by the tumour mass immediately after the infarction. The swelling must have subsided, however, since there was no sellar distension or cavernous-sinus displacement at operation in the first case and no striking tension of the optic pathways in the second. The right hemiparesis and initial dysphasia—presumably caused by circulatory disturbance in the territory supplied by the middle cerebral artery—recalls the hemiplegic presentation of Schnitker and Lehnert's patient (1952).

The electrolyte disturbance in pituitary apoplexy has received little comment in the past, though the fall in blood-pressure has been mentioned often enough. These hypoadrenal effects, which were mild in our first patient and severe in the second, are important; and in the days before corticoid therapy inability to correct them probably contributed to the high death-rate.

The unusually severe meningeal irritation and cerebrospinal-fluid pleocytosis in the second case aroused suspicions of pyogenic infection; but the meningitis must have been chemical, and due to contamination of the subarachnoid space by necrotic tumour material. The patient's deep depression of consciousness, fading into persistent forgetfulness and mental hebetude, bespeaks a basal cerebral disorder, doubtless caused by hypothalamic compression or irritation.

In neither of our cases is it possible to estimate the age of the tumour accurately. If the delayed adolescence and weak beard-growth of the first patient and the scanty secondary hair and poor response to cold of the second can be relied on as guides, then thirty years or more is the answer. On the other hand, such endocrine symptoms may be expressions of a lifelong genetic pituitary dyscrasia which may only later stimulate the development of an adenoma (Antony Jefferson 1957). In our first case there is a hint of familial pituitary hypofunction: the patient said that his grandfather had to shave only seldom.

The idea has gained currency that infarcts are commoner in eosinophil than in chromophobe adenomas, but perusal of the literature suggests the reverse. This would not be surprising, since the chromophobe variety is commoner. Our second case belonged to it, but in our first case no pituitary tissue could be identified. (The patient had somewhat coarse features but he was not frankly acromegalic; and chromophobe tumours may contain areas of eosinophilia.)

Summary

Two cases of massive spontaneous infarction in a pituitary adenoma are described.

This diagnosis should always be borne in mind when patients with pituitary dysfunction suddenly develop signs of an intracranial catastrophe—subarachnoid hæmorrhage, meningitis, blindness, ocular palsy, or collapse with coma. There may have been no previous symptoms of a pituitary tumour.

The pathogenesis and management of such cases is discussed.

We are glad to record our thanks to Mr. R. D. Weeden Butler, D.O.M.S., who referred the first patient to us, and to Dr. S. R. F. Whittaker, F.R.C.P., who referred the second.

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WERNICKE'S ENCEPHALOPATHY ASSOCIATED WITH DIGITALIS POISONING

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THE following case is believed to be unique in that Wernicke's encephalopathy resulted from protracted vomiting and anorexia due to digitalis poisoning.

A married woman, aged 56, was admitted to the Royal Infirmary, Edinburgh, on March 8, 1958, because she had been vomiting frequently, had become increasingly weak, and for about five days had been mentally disturbed.

On examination she was completely disorientated. The skin was warm and moist but pale. The peripheral pulses were rapid and bounding and the heart sounds loud—signs which were in striking contrast to her apathetic appearance. The bladder was distended almost to the level of the umbilicus; the bowel was incontinent. The range of upward and downward conjugate deviation of the eyes was full, but lateral movement to either side was absent. The muscles of the forearms, hands, and legs were obviously wasted. All movements were weak, and mild foot-drop on the left side was noted. With the exception of the biceps jerks, the deep reflexes could not be elicited. The calf muscles were exquisitely tender on pressure.

Diagnosis.—The patient was considered to be suffering from a deficiency of thiamine, and Wernicke's encephalopathy was diagnosed. This diagnosis was supported by the finding of a serum-pyruvate level of 1·6 mg. per 100 ml. (the upper limit of normal for the laboratory which undertook this test is 1·2 mg. per 100 ml.).

Previous record.—A remarkable story, which led to the cause of the syndrome being established, was obtained by questioning the patient's relatives, the family practitioner, and the local chemist. The patient had been strong and healthy until July or August, 1957. She then began to worry over trivialities, became emotional and domineering, and complained of palpitations. She had been disinclined to eat and had lost a little weight. After witnessing a fatal road accident in the last week of December she was greatly distressed and developed violent palpitations which lasted for more than forty-eight hours. Her doctor found the pulse to be rapid and irregular, and considered that she had auricular fibrillation. Tablets of digitalis leaf 0·1 g. thrice daily were prescribed. About a week later, anorexia became complete and the patient started to vomit. She continued to take the digitalis tablets for more than two months. She vomited at least once daily from the beginning of January to the beginning of March, 1958 (i.e., until ten days after the digitalis was stopped). During this period large quantities of a proprietary beverage containing glucose were consumed, but little or no solid food seems to have been retained. The patient lost more than 5 stone in weight after October, 1957, mostly in the few weeks before admission to hospital. That much of the digitalis taken must have been assimilated was confirmed by characteristic changes in the electrocardiogram three weeks after the last tablet had been ingested.

Treatment and progress.—Treatment with thiamine was instituted. The patient received initially 100 mg. intravenously, 50 mg. by intramuscular injection three times a day in the next two days, and thereafter 25 mg. daily by mouth. Within twenty-four hours ocular movements were restored, and coarse nystagmus on lateral deviation of the eyes became apparent. Because of improvement in her mental condition it was possible in the next few days to demonstrate more clearly the features of Korsakoff's psychosis. She showed gross memory impairment for recent events, confabulation, perseveration, and total disorientation for time and place. By the tenth day of treatment the patient's appetite was returning, bowel and bladder function was normal, the knee-jerks could be elicited, and she was quieter. This clinical improvement had resulted from the administration of thiamine, which was the only dietary supplement. Since, however, her dietary intake of many factors must have been deficient she received, at this stage, three daily injections of a multi-vitamin preparation (' Parentrovite ').

Recovery was slowed by urinary infection, femoral-vein thrombosis, and parotitis, but by May 23 the patient was fit to return home. Apart from absent ankle-jerks there was now no sign of peripheral neuritis; muscle power was good and she was ambulant. Memory impairment of the Korsakoff type persisted but orientation was normal. Despite a good appetite, no weight had been gained, and the resting pulse-rate remained rapid (90–110).

The patient was seen again on June 25. Mental function had clearly improved further. Although she made several errors in simple arithmetical tests and was slow of performance, she now remembered most of the events leading up to her admission to hospital and she no longer confabulated. Electroencephalograms obtained at the height of the illness (March 23) and later during her stay in hospital (May 3) showed considerable delta activity over the frontal regions of the brain, while the record taken on June 25 was normal.

The patient was, however, still complaining of fatigue; her weight had remained stationary despite a good appetite; she was excited and talkative; her hands were hot and moist, and her outstretched fingers were tremulous; she was intolerant of warmth; and tachycardia (pulse-rate 110–120) was persisting. Accordingly tests of thyroid function were undertaken, and these confirmed the clinical impression that the patient had thyrotoxicosis. No doubt the palpitation for which the digitalis was originally prescribed was due to this cause. A therapeutic dose of radioactive iodine was given, and a satisfactory outcome is expected.

Discussion

The acute superior hæmorrhagic polioencephalitis of Wernicke was at one time believed to be confined to alcoholics. But one of the three patients originally reported by Wernicke (1881) was a seamstress, aged 20, whose death resulted from intractable vomiting shortly after she had attempted suicide by drinking sulphuric acid.

Between 1932 and 1938 cases of Wernicke's disease due to various other causes were reported—e.g., polyneuritis gravidarum (Berkwitz and Lufkin 1932, Tillman 1934, Wagener and Weir 1937); a cerebral disorder ascribed to " milk intoxication" in suckling infants (Tanaka 1934); and gastric cancer (Neuburger 1936). Later the classical experiments of Alexander et al. (1938, 1940) in pigeons, and the accounts by Campbell and Russell (1941) in this country and Jolliffe et al. (1941) in the United States, of the specific therapeutic effects of thiamine in man, established that thiamine deficiency was the main ætiological factor.

Campbell and Russell (1941) studied cases where death had followed vomiting due to gastric cancer, pyloric stenosis, and pregnancy. One of their cases was a $3^1/_2$-month-old infant who developed anorexia and occasional vomiting in association with whooping-cough. The disease has also been observed in patients with anorexia due to mental illness (Jolliffe et al. 1941); in prisoners-of-war in Singapore with a deficient dietary intake whether suffering from dysentery (de Wardener and Lennox 1947) or not (Cruickshank 1950); in malnourished infants with infections (Guerrero 1949); and in patients with disordered gastrointestinal absorption (Dommann 1952). From these reports it appears that Wernicke's encephalopathy may develop in any condition precipitating acute deficiency of thiamine.

Conclusions and Summary

In this case Wernicke's encephalopathy developed in consequence of anorexia and persistent vomiting due to digitalis poisoning. The thiamine deficiency may have been aggravated by the taking of large quantities of glucose drinks during a period when no solid food was being retained and also by thyrotoxicosis. Biochemical evidence that thyrotoxicosis may cause thiamine deficiency has been obtained experimentally (Peters and Rossiter 1939) and in patients with thyrotoxicosis (Williams et al. 1943).

Despite persistent vomiting, the patient continued to take her digitalis tablets as prescribed. William Withering (1785) fully appreciated some of the unfavourable actions of the drug which he introduced. With foresight he states that he was prompted to write *An Account of the Foxglove* lest the lives of men be "hazarded by its unguarded exhibition ".

I wish to thank Prof. D. M. Dunlop, under whose charge the patient was investigated and treated, for permission to publish.

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Preliminary Communication

SERUM-ALBUMIN CATABOLISM AND NITROGEN EXCRETION

THE quantity of nitrogen excreted by patients recovering from various forms of injury often exceeds that found in normal people (Cuthbertson [1]). During an investigation of the metabolism of albumin in these patients it was observed that the rate of albumin catabolism was also raised. Sterling et al.[2] found a raised rate of albumin catabolism and of nitrogen excretion in patients undergoing major surgical procedures but thought that the two rates were not closely related. The present study was made to explore the correspondence between the rate of nitrogen excretion and the rate of albumin catabolism in patients with different clinical conditions.

CLINICAL MATERIAL

Three patients were studied in detail:

CASE 1.—A woman of 22 with about 25% of her body surface burned—most of it whole-skin loss.

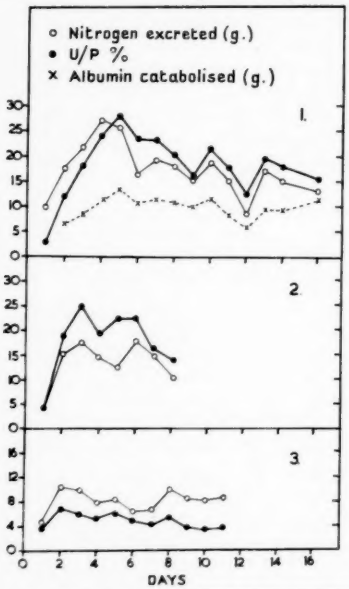
CASE 2.—A man of 26 with fractured femur, fractured tibia and fibula, fractured radius and ulna, and facial lacerations following a road accident.

CASE 3.—A woman of 35 with chronic hepatitis and ascites. Her serum-albumin level was 1·9 g. per 100 ml.

METHODS

Human serum-albumin (Lister Institute) was labelled with ^{131}I to a level of 1μC per mg. protein and to less than one atom of iodine per protein molecule. Less than 2% of the radioactivity in the final product was present as free iodide ions. After intravenous injection of the labelled albumin the radioactivity per ml. of plasma and of 24-hour urine samples was measured in a scintillation counter. Nitrogen in urine was determined by the micro-Kjeldahl method. Plasma samples were taken at about the mid-point of the urine collection periods.

Some 60–80% of the albumin from each plasma sample of case 1 was separated by a cold-alcohol fractionation technique. Electrophoresis in starch gel showed that this albumin was almost completely free of globulins. After determination of the concentration of albumin by the Folin-Ciocalteau method and measurement of the radioactivity, the specific activity in counts per minute per mg. albumin was available. The amount of albumin catabolised per day was calculated from the total urinary radioactivity and the specific activity of the albumin in the appropriate plasma sample (see figure).



1. Cuthbertson, D. P. *Biochem. J.* 1930, **24**, 1244.
2. Sterling, K., Lipsky, S. R., Freedman, L. J. *Metabolism*, 1955, **4**, 343.

An alternative approach is described by Veall and Vetter [3] where the ratio (U/P) of total radioactivity in a 24-hour urine sample is compared with that in the plasma (plasma volume × counts per minute per ml.) for each day. This procedure has the advantage of convenience and does not require daily albumin determinations. The results express catabolism as the proportion rather than the quantity of circulating albumin broken down. The ratio U/P for each of the three cases is shown in the chart with the total amounts of nitrogen excreted.

RESULTS

As may be seen, there is close correspondence between the timing of changes in albumin catabolism and in total nitrogen excreted. The rates also showed a striking proportionality; in cases 1 and 2 the rate of albumin catabolism was between two and three times the normal value of 9% per day, whereas in case 3 it was only half the normal. Total protein catabolism—as shown by nitrogen excretion—was about twice the normal value of 10–15 g. per day in cases 1 and 2 and about half the normal value in case 3. The catabolism of albumin contributed about 9% of the total nitrogen in the urine.

DISCUSSION

Cohen et al.[4] have shown that the iodine label of iodinated albumin is not reutilised in protein synthesis but is excreted quantitatively in the urine, provided the thyroid gland is saturated with inactive iodide. Carefully iodinated albumin is almost certainly metabolised at the same rate as unlabelled albumin. The radioactive iodide excreted is therefore a valid indication of albumin catabolism.

Our results illustrate a remarkable correspondence between changes in albumin and in general protein catabolism, both in respect of direction of change and in respect of general proportionality. The agreement continued throughout the 1–2 weeks of the experiments. Blythe et al.[5] imply that similar relationships may occur after administration of hydrocortisone. Although exceptions to this parallelism may be found, it seems that in the widely differing clinical conditions of burns, multiple injuries, and cirrhosis some common mechanism controls alike the catabolism of albumin and of total protein. This finding may also have useful applications in studies of nitrogen metabolism in various disease states, and in tests of the action of hormones and other agents.

We wish to thank Mr. D. M. Jackson, Mr. Henry Proctor, Dr. P. W. Dykes, and Dr. P. G. Arblaster for permission to publish data on patients under their care.

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3. Veall, N., Vetter, H. Radioisotope Techniques in Clinical Research and Diagnosis; p. 318. London, 1958.
4. Cohen, S., Holloway, R. C., Matthews, C. M. E., McFarlane, A. S. *Biochem. J.* 1956, **62**, 143.
5. Blythe, W. B., Iber, F. L., Werner, I., Rubini, M. E., Frick, P. G., Meroney, W. H. *Clin. Res. Proc.* 1957, **5**, 190.

"... The practice in hospital appears to be to ignore all the jobs which a housewife does in spring cleaning and then when conditions are bad to repaint or replace. Much money would be saved if thorough cleaning was done regularly and such things as stair carpets moved at intervals. Surely a group of semi-skilled people could be employed on these jobs the year round in a hospital group. I wonder at times why State registered nurses had to attend lectures on hygiene if it is to be regarded only as a theoretical subject."—RITA GRENVILLE MATHERS, *The Times*, Jan. 28, 1959, p. 9.

Medical Societies

MANCHESTER MEDICAL SOCIETY

Developments in Radiotherapy

ON Jan. 13 Prof. J. S. MITCHELL (Cambridge) described to the section of surgery some of the laboratory and clinical studies which he and his colleagues have carried out. He dealt with five main problems:

(1) The nature of the selective damage to tumour cells in radiotherapy is associated with the disturbance of nucleic-acid metabolism following therapeutic doses of radiation. The process of inhibition of synthesis of desoxyribose nucleic acid, or of its initiation, is not per se the most radiosensitive step, although closely related to it. He suggested that the most important mechanism is a "macromolecular lesion" of desoxyribonucleoprotein.

(2) In a study of the microscopic spread of malignant tumours the bone-marrow has been examined in 600 patients with various types of malignant disease, especially in the early stages. The prognosis is worst in cases with tumour cells in the marrow; in carcinoma of the bronchus, cervix uteri, and ovary, marrow plasmacytosis is associated with a poorer average survival than is a normal marrow.

(3) Isotope therapy raises great problems. Thus, a major difficulty is inhomogeneity of the distribution of the radioactive isotope and of the radiation dose after internal administration. Professor Mitchell described a study of the use of an alternative isotope of iodine—^{124}I—in the treatment of inoperable cases of carcinoma of the thyroid.

(4) An attempt has been made to obtain further information about the mechanisms of the therapeutic actions of radiations by the study of chemical radiosensitisers, especially tetra-sodium 2-methyl-1 : 4-naphthohydroquinone diphosphate ('Synkavit') and related compounds, and oxygen. Tissue-culture studies were made with 152 compounds; animal experiments with the Walker rat carcinoma, using 12 of these; and clinical trials with 3 of the compounds (synkavit, the related 2 : 3-dimethyl derivative, and tetra-sodium 2 : 3 : 6-trimethyl hydroquinone diphosphate). For radiosensitisation the compound must be injected intravenously, and the timing of the injection before irradiation is critical. Apparently the radiosensitiser acts by increasing the dose of radiation effective in the tumour cells, sometimes by about 60%. From a practical point of view the radiosensitiser makes it possible to increase the volume of tissue irradiated to a level of dose corresponding to the region of optimal dose; there is usually no improvement in the results of radiotherapy at levels of radical dosage.

(5) Finally Professor Mitchell described studies of high-energy radiations in radiotherapy with especial reference to 30 MeV X rays.

New Inventions

A PUMP FOR EXTRACORPOREAL CIRCULATION

OUR previous work with a number of pumps of industrial type indicated that the 'Mono' pumping principle, embodying a helical stainless-steel rotor revolving in a stator of resilient material, was satisfactory for use with an extracorporeal circulation.[1] This principle uses rotary motion to move a seal continuously through the stator at uniform velocity to give positive flow. The seal is constantly recreating itself at the inlet, or suction end, of the pump by the cooperating engagement of the helical rotor with the stator, which is of similar helical formation but is twice the pitch of the rotor (fig. 1).

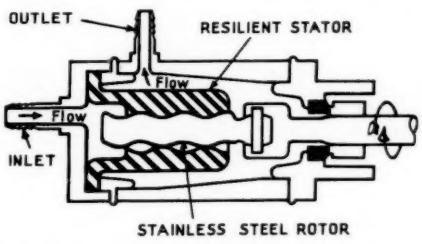

Fig. 1—A sectional arrangement of the Ormond-Mono pump for extracorporeal circulation.

As the pumping action is produced by rotary motion, the flow-rate is proportional to the speed of rotation, which makes calibration of the pump simple.

Although the industrial-type mono pump was satisfactory in principle, it had three disadvantages when used in a human extracorporeal circuit:

1. The method of dismantling for sterilisation was not suitable for hospital practice.

2. Small quantities of air, entrapped during initial priming, could not easily be expelled.

3. The industrial grade of stator might have toxic properties with human blood.

1. Hall, J. E., James, P. A., Lucas, B. G. B., Waterston, D. J. *Thorax*, 1958, **13**, 34.

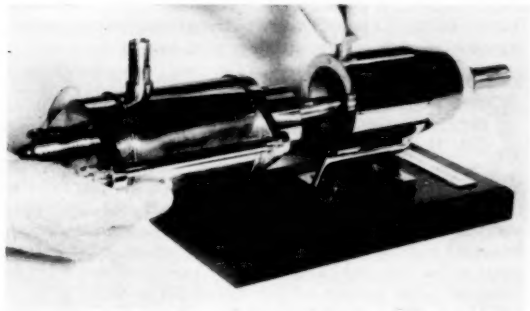

Fig. 2—The autoclaved pump cartridge is easily fixed to the driving mechanism without the use of tools.

The pump was therefore modified. (1) The unit was engineered in stainless steel and redesigned in such a way that it could be dismantled without tools, and the pump section could be autoclaved in one piece. This was achieved by separating the pump from the driving mechanism to form a pump cartridge, which could be simply attached to the driving mechanism by a pin through the driving shaft (fig. 2). (2) The liquid housing was reshaped to assist the evacuation of air when filling the system. (3) The resilient stator was moulded in specially compounded polyvinyl chloride.

This pump has been thoroughly tested and found to have a hæmolysis-rate similar to that of the industrial model. In use, it has proved to be entirely satisfactory.

This pump will shortly be available from Mono Pumps Ltd., Sekforde Street, Clerkenwell Green, London, E.C.1, to whom we are greatly indebted for their valuable help and cooperation with this modification, and especially to Mr. E. Alcock, their chief research engineer.

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B. G. B. LUCAS
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The Cardiac Research Unit,
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Reviews of Books

The Preservation of Eyesight

Sir ARTHUR SALUSBURY MACNALTY, K.C.B., M.A., M.D. Oxon., F.R.C.P., F.R.C.S., formerly chief medical officer of the Ministry of Health and Ministry of Education. Bristol: John Wright. 1958. Pp. 107. 12*s*. 6*d*.

IT is remarkable that, at a time when the number of registered blind is increasing appreciably, the knowledge of ocular disease expected of the undergraduate at qualifying examinations should be so slight. Occasional (and usually optional) questions appear in most final-examination papers; but, with one or two notable exceptions, the doctor's responsibilities in the prevention of blindness are not emphasised by adequate examination at this stage. That the advice which many general practitioners can give in cases of serious ocular disease is limited, especially when blindness threatens, is perhaps not surprising. Partly from these circumstances springs the need for literature on eye disorders, couched in simple terms and addressed primarily direct to the lay public. This small volume, compiled by a consultative committee of experts under distinguished editorship, is especially welcome. It is written in simple language, intelligible to laymen but acceptable to the medically educated. In its fourteen brief chapters it gives a lucid outline of the ocular anatomy, defects and diseases of the eyes, the effect of varied lighting conditions on vision, the prescribing and use of spectacles, and the care of the eyes in general. Welfare facilities for the blind are noted in a separate section; another useful chapter is devoted to industrial diseases and injuries. The book will undoubtedly prove valuable to the general practitioner, the industrial medical officer, and interested laymen.

Rehabilitation of the Hand

C. B. WYNN PARRY, M.B.E., M.A., D.M., D.PHYS.MED., specialist in physical medicine, R.A.F. London: Butterworth. 1958. Pp. 293. 45*s*.

TEN or twelve years ago a surgeon particularly interested in the hand might have accommodated all the textbooks on that subject on a single shelf. Today such books have multiplied, and yet there are still gaps; until now, for instance, no volume has dealt in detail with the postoperative or conservative treatment of the damaged hand. Squadron-leader Wynn Parry has provided a full account of the restoration of function to the crippled hand by methods which have been tested and proved in his own unit. The only serious reservation is that he describes the rehabilitation of injuries under almost ideal conditions, and some of the methods advocated (involving up to three months' attendance in a special physiotherapy unit) are, unfortunately, not applicable in ordinary civilian circles. But this work does provide the surgeon, working without such facilities, with praiseworthy examples of the results which can often be obtained in unpromising cases, and with clear instructions on how he may emulate them.

Electrolyte Changes in Surgery

K. E. ROBERTS, M.D., assistant chief of medicine, United States Public Health Service Hospital, assistant professor of medicine, Stanford University College of Medicine; P. VANAMEE, M.D., assistant attending physician, Memorial Hospital, New York; J. W. POPPELL, M.D., chief, section of cardio-pulmonary physiology and associate, Sloan-Kettering Institute for Cancer Research, New York. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1958. Pp. 113. 34*s*.

THIS small monograph deals not only with subjects usually encompassed by a book on electrolyte problems in surgery, but also with some other metabolic problems such as the dumping syndrome, hepatic failure, and renal disease. With such a wide scope the information in each section must necessarily be brief, and this difficulty is exacerbated by the length of the section on disturbances in acid-base balance, which occupies nearly half the book. This main section contains a detailed account of the changes in acidosis and alkalosis, with emphasis on metabolic as opposed to respiratory disturbances. The serious student of these disturbances will find this survey a useful if strenuous introduction; but the clinician, for whom this book is written, will undoubtedly find it very hard going. The sections on the administration of fluids before and after operation are extremely brief and contain no reference to the diagnosis and treatment of established deficits. There is a good bibliography but no index, and even in these days the price seems excessive.

The Comparative Anatomy and Physiology of the Nose and Paranasal Tissues

Sir VICTOR NEGUS, HON. D.SC. Manc., M.S. Lond., F.R.C.S., HON. F.R.C.S.E., HON. F.R.C.S.I., consulting surgeon to the ear, nose, and throat department, King's College Hospital, trustee of the Hunterian Collection. Edinburgh: E. & S. Livingstone. 1958. Pp. 402. 70*s*.

IN this new book Sir Victor Negus has produced a companion for his much-admired work on the larynx. As in his earlier work, he discusses the lessons to be learnt from comparative anatomy and physiology. This he does both as biologist and as clinician; and so well does he communicate his enthusiasm that the reader may be left with an urge to revisit not only the museum of the Royal College of Surgeons but also the zoological gardens in Regents Park. Most rhinologists will want to read this book, and will find it good reading; but it will appeal also to anatomists and zoologists.

Recent Advances in Cerebral Palsy

Edited by R. S. ILLINGWORTH, M.D., F.R.C.P., D.P.H., D.C.H., professor of child health, University of Sheffield. London: J. & A. Churchill. 1958. Pp. 389. 50*s*.

UNLIKE other volumes in the Recent Advances series, which present modern news and views of recent work in a specialised subject, this work gives a conspectus of authoritative information. In fact, it is the only textbook on the subject, despite Professor Illingworth's denial of this intention in his foreword. The book is easily read and not over-long. The editor has succeeded in coordinating a team from all over the world and has persuaded them to write constructively rather than reminiscently. The practical advice to be found here will be valuable to all interested in the subject.

Electrocardiogram Clinics

JOSEPH E. RISEMAN, M.D., assistant clinical professor of medicine, Harvard Medical School; visiting physician, Beth Israel Hospital, Boston, Mass. ELLIOT L. SAGALL, M.D., instructor in medicine, Harvard Medical School; assistant visiting physician, Beth Israel Hospital, Boston, Mass. London and New York: Macmillan. 1958. Pp. 259. 73*s*. 6*d*.

THE preface states that the purpose of this book is to illustrate the practical use of the electrocardiogram in the management of patients with definite or suspected heart-disease. Each case-history is given in detail, and the electrocardiogram is reproduced full-scale; the history and electrocardiogram are then discussed in detail, and further sections are given to the clinical correlation and to questions. While the approach is realistic it makes for wearisome reading, and there are probably few physicians in this country who would not prefer to spend their reading time for electrocardiography on a more condensed account and to obtain their experience in their own patients.

Clinical Involvements, or The Old Firm. (London: Butterworth. 1958. Pp. 200. 32*s*. 6*d*.).—Dr. H. Gardiner-Hill recounts here the histories of some patients he has seen, drawing lessons and pointing morals from them. Young practitioners will find here help in some of their clinical problems, and St. Thomas's men will enjoy reading about remembered cases. The pages are enlivened by some amusing line drawings.

Hæmatological Technique (2nd ed. London: J. & A. Churchill. 1958. Pp. 244. 24*s*.).—In the first edition of this book, designed for technicians taking the I.M.L.T. examinations, Dr. E. M. Darmady and Mr. S. G. T. Davenport included nothing about blood-groups. This omission has been remedied by the addition of four chapters on blood-groups, cross-matching, and serology. The rest of the book has been revised; but there is still no account of photoelectric hæmoglobinometry.

THE LANCET

LONDON 14 FEBRUARY 1959

The Ministry

WE agree with Sir GEORGE SCHUSTER that

"The establishment and working of the National Hospital Service in these first ten years represent notable achievements. . . . But there has been a good deal of provisional 'muddling through' and there are points of weakness and insecurity which justify anxiety for the future. The time has come for a general overhaul and tuning up of the administrative machine. . . ."

The Acton Society's concluding report,[1] from which these words are taken, is a frank, fair, and constructive study of the shortcomings of the Ministry of Health as the central authority for the hospitals. As the body to which the hospitals are responsible, the Ministry's task is to exercise control: as the body which is responsible for the hospitals, it should provide leadership and guidance. The exercise of control is not, of course, a merely negative function, and the report approves on the whole the way in which the Ministry has positively influenced the development of the hospital service by altering the distribution of money between regions and by setting sums aside for specific purposes such as the improvement of mental hospitals. Granted that the basis of its financial control had to be empirical, it has acted sensibly—though perhaps it has not done enough to get away from empiricism and find means whereby the money a hospital receives is more closely related to what it achieves, both in quantity and quality. But if, judged by results, control over development has been reasonable, it could perhaps have been exercised more efficiently: the time taken for examining major projects is often embarrassingly long, and there is excessive scrutiny of details which ought to be left to the hospital boards and committees even at the risk of occasional mistakes.

This report, however, is chiefly concerned with the Ministry's other function—leadership. Here the evidence is more nebulous, but throughout the hospital service there is an unmistakable impression of "a lack of helpful leadership at the top". The Ministry's officers, it is felt, "adopt too passive a role, tending to continue, as in the days of the Local Government Board and of conditions before 1948, to exercise purely regulatory functions . . .". The Select Committee on Estimates were not satisfied that the Ministry had always acted with vigour and foresight in using its powers of planning, guiding, and advising. In defence of the Ministry, the Acton Society points out that "ambitious strategic planning based on inadequate knowledge can be extremely dangerous", and says that if, with generous capital resources, our hospitals had been developed on plans made ten years ago, much money might have been wasted for needs change with the advance of science. On the other hand, the Ministry may be criticised for not doing enough to collect the new knowledge on which accurate planning must depend, and also for giving too little guidance based on the considerable amount of work that has in fact been done:

". . . the criticisms which seem to us to deserve consideration are that the Ministry tends to refer problems to advisory committees and then to content itself with publishing their reports without comment; alternatively that when the Ministry does issue advice this is given through Ministry circulars and is less helpful and effective than it could be. . . . Reliance on committee reports and guidance by circular is not good enough. The Ministry's own staff should be more concerned with watching the whole front so as to maintain awareness of all matters on which helpful advice is required; to see that the knowledge on which such advice is based is co-ordinated and kept up-to-date, and above all to watch how the advice given is followed up. The Ministry should have staff qualified to perform these tasks and to maintain understanding liaison with the hospital authorities."

As the apex of a service which is intended to combine the advantages of concerted action with those of free initiative, the Ministry is delicately placed; and in these first ten years, Sir GEORGE SCHUSTER says,[2] "it has been far better to have too little interference than too much from the central authority". For the future he would have the Ministry follow the principle of government which JOHN STUART MILL expressed in his *Essay on Liberty*: "The greatest dissemination of power consistent with efficiency; but the greatest possible centralisation of information and diffusion of it from the centre." For collecting and diffusing information the Guillebaud Committee recommended that the Ministry should have a research and intelligence department: this should be "constantly engaged in the search for facts and information which would enable administrators to make right decisions for the future development of the Service: above all, it should be looking out for the right sort of questions that ought to be asked".[3] Sir GEORGE sympathises with the Ministry's wish to feel its way—it has started a statistical section on a small scale—but he would himself go even further than the Guillebaud Committee. Something more is required, he holds, than a central intelligence department regarded as a detached piece of machinery working on its own account or as a tool to be used occasionally by the executive staff:

"The Intelligence Staff must be an integral part of the executive. It must have its own creative role as a detector of problems and a productive source of wisdom, and its integration with the executive staff should be such that the governing and creative functions of the Ministry can work together in harmony."

The lack of an intelligence staff cannot be made good by the Minister's advisory bodies, whose "product is reports, something very different from action". Recognising that the Central Health Services Council, in particular, has done extremely valuable work, Sir

1. Hospitals and the State. Paper no. 6: Creative Leadership in a State Service. London: Acton Society Trust, 39, Welbeck Street, W.1. 1959. Pp. 80. 4s. (postage 6d.).

2. *ibid.* part II.

3. Report of the Committee of Enquiry into the Cost of the National Health Service; p. 234. Cmnd. 9663. H.M. Stationery Office, 1956.

GEORGE quotes our remark [4] that it has never become, as originally intended, the brain of the National Health Service, but declares that this intention was wrong: "the 'brain' of the service must be an integral part of its whole body—not a part-time detached instrument". He conceives of the intelligence staff within the Ministry as concerned with the social as well as the medical aspects of hospital care—with hospitals in their social setting. Obviously such a staff would do little good unless it could command the services of men with the right qualities of wisdom combined with knowledge of medical affairs; and, though he believes that men can be found in our profession who could answer the new needs created by the N.H.S., and think in terms of its wider implications, he points out that "someone in authority must sound the call for their wisdom and open the opportunity for them to bring it to bear on the conduct of the service".

The report speaks repeatedly of the need for the hospitals service to build up a staff of able administrators, both medical and lay, and to bring people with field experience into the Ministry. On the Civil Service side, this department, with its diminished prestige, has nowadays less attraction for the best young entrants, and this has increased the immense burden of routine which at present prevents many of their seniors from doing the things they ought to be doing. Sir GEORGE SCHUSTER thinks that "the whole work of the Ministry should now be subjected to independent expert investigation so as to examine how far efficiency could be improved and the volume of clerical work reduced by increasing the discretion allowed to the lower formations, by cutting out unnecessary returns, and by eliminating the delays and voluminous correspondence involved in the querying of minor points". But evidently he also believes that the service is short of talent. A small investigation by the Acton Society's research staff suggests that the proportion of "top management" posts in the hospital service, from the Ministry downwards, is far below what is usual in large business organisations—and that many people in the service doing what should be classified as top-management jobs get far less than the appropriate pay. Answering in advance the argument that recruitment of able people is expensive, and that his proposals "imply a stepping up of the power and managerial function of the Ministry", he quotes MILL again: "A Government cannot have too much of the kind of activity which does not impede, but aids and stimulates execution and development." He wants to see the Ministry so staffed that it can place more emphasis on "aiding and stimulating" and less on the "impeding" process of regulative checks and queries. If this were brought about, the increase in the number of people at the top, qualified to give creative stimulation, might be balanced by a considerable reduction in the lower ranks who perform regulative functions.

Finally Sir GEORGE SCHUSTER provides some very interesting answers to a question which we raised last summer [4] when we asked why the Minister who looks after the Health Service need have a department so unimaginatively similar to other Government departments. Believing that the Ministry is unlikely to give understanding leadership unless top posts on its staff are filled by people with practical experience of hospital administration at the operational level, he would open these central posts to men and women who show outstanding ability at the periphery. The first step might most conveniently be to arrange temporary interchange of staff, as done of late years by the Colonial Office, which has benefited by bringing members of the Overseas Civil Service to Whitehall and seconding its own officers to posts abroad. But the more radical change that Sir GEORGE proposes is that the Ministry of Health should be reconstructed on the lines of a Service Ministry, in which the operating Service (Navy, Army, or Air Force) is fitted into the established pattern of Whitehall but remains under the direction of its own officers. The War Office, for instance, has its civil division directed by the Permanent Under-Secretary, but on the same level it has three military departments (directed by the Chief of the Imperial General Staff, by the Adjutant-General, and by the Quartermaster-General) which are almost exclusively staffed by the Army. On this analogy, the Ministry of Health might have two senior posts for the hospital service, one corresponding to that of C.I.G.S. and the other to a combination of A.G. and Q.M.G.: for the former the normal line of succession would be through the senior administrative medical officer posts in the regions, and for the latter it would be through the lay administrative service. Possibly chief officers on the same level could be appointed for each of the other two arms of the National Health Service, and a coordinating body might emerge analogous to the Chief of Staffs Committee of the three Services. Sir GEORGE refrains from going into details because he does not want to distract attention from the basic idea—which is that, by taking thought, an operating service can work under the direction of its own officers while remaining in the necessary relationship with Minister and Civil Servants.

These military parallels are at first sight disturbing. The hospital service is not a hierarchical organisation like the Army: indeed it is not really a service at all, but a federation of largely self-governing institutions. It is in the "institution", large or small, that medical work is done; and (as Sir JAMES SPENCE pointed out [5]) it is to his hospital, not to any centralised "service", that the doctor gives his time, his thought, his loyalty. But Sir GEORGE SCHUSTER, too, is very well aware of that: he wants the members of hospital boards and committees to have more real responsibility, and he wants to know how the working of the national service is reacting on our profession, "especially in regard to its scope for the realisation of its own highest ideals". Professional and even administrative freedom are not, he holds, inconsistent with the kind of central leadership he has advocated; and in hospital work such leadership

4. *Lancet*, 1958, ii, 27.

5. Spence, J. C. (posthumous paper) *ibid.* 1955, i, 41, 31.

would certainly be more acceptable if it came from people who were professional and administrative colleagues. As for the other parts of the National Health Service—general practice and the work of local authorities—we hold that nothing like enough has yet been done to consider their role and development in relation to that of the hospitals. To secure unity of effort between the three divisions of the service is, as the Acton Society says, a " well-known problem, the full solution of which may depend on some drastic reorganisation and rearrangement of departmental responsibilities ". On such large issues, as on small ones, an attempt should always be made to answer Sir GEORGE's three questions: " What are we trying to do? Is it worth doing? And, if so, is this the best way of doing it? " The Ministry of Health has done much fine work, and has often shown remarkable wisdom, in the very difficult years since the service started. But it was not originally designed either for the administration of a huge and technical undertaking or for answering the kind of questions on which success therein will ultimately depend. The time has come, surely, to think of remodelling it for what it has to do *now*, and in the future.

" Protein-losing Gastroenteropathy "

GENERALISED œdema affecting the arms and legs, accompanied by transudation into serous cavities, is thought to arise chiefly in three ways: from raised venous pressure, as in constrictive pericarditis or tircuspid incompetence (although this is usually associated with cardiac cirrhosis); from increased permeability of capillary walls, as in beriberi or epidemic dropsy [1] and perhaps acute glomerular nephritis; or from lowered osmotic pressure of the plasma. In this country when a patient presents with generalised œdema—as opposed to œdema developing during another illness—lowered osmotic pressure is much the most likely explanation.

It has long been known that the most important constituent maintaining the tonicity of the plasma is albumin. And studies with ^{131}I-labelled human serum-albumin have resulted in distinction of two large groups of low-albumin states—those in which albumin formation is decreased, and those in which albumin loss is increased.[2] The most important members of the first group in Western countries are hepatic cirrhosis and the sprue syndrome; but in a world series famine œdema from failure of protein ingestion would head the list. Much protein may be lost in the nephrotic syndrome; and most of what is lost is albumin in this condition, which has been referred to as " high-output liver failure ".[3] Generalised œdema may also be associated with other protein-losing diseases, such as bronchiectasis, ulcerative colitis, and exfoliative dermatitis; and here the exact mechanism of hypoalbuminæmia has hitherto not been clear.

In addition, a few patients present with œdema, and yet appear to eat and absorb protein and synthesise albumin adequately, and show no evidence of protein loss. This condition, which was probably first recognised by CSÉPAI [4] in 1923, is commoner in children than adults, and œdema is the chief and often the only sign. The serum-albumin is always lowered, sometimes greatly, and the serum-cholesterol is never increased. The patient sometimes recovers spontaneously. At necropsy no lesion can be found to account adequately for the low serum-albumin; and COPE and GOADBY [5] suggested that it might be due to increased internal protein loss. In 1949, however, ALBRIGHT et al.[6] showed a greatly increased rate of disappearance of intravenous ^{131}I-labelled human serum-albumin, and this finding has since been confirmed by others. CITRIN et el.[7] studied a patient with hypertophic gastritis associated with hypoproteinæmia and œdema and detected a notable loss of ^{131}I-labelled albumin into the stomach. Similar alimentary protein loss has since been demonstrated in ulcerative colitis and regional enteritis.[8]

Now a great advance has been made. Dr. GORDON, whose paper appears on p. 325 of this issue, has succeeded in labelling polyvinylpyrrolidone (P.V.P.) with ^{131}I. This substance, with a molecular weight of about 40,000, is unaffected by proteolytic enzymes and is in widespread use as an artificial plasma substitute. Dr. GORDON's report, and that by Dr. SCHWARTZ and Dr. JARNUM (p. 327), show that ^{131}I-P.V.P. is extremely valuable for measuring the permeability of the alimentary tract to serum-proteins. GORDON,[9] after carefully standardising the test, has measured fæcal ^{131}I-P.V.P. after a single intravenous injection in 9 patients with " idiopathic hypercatabolic hypoproteinæmia ". In all of them alimentary loss was greatly increased. These results are confirmed in 4 further cases by SCHWARTZ and JARNUM, who also report a case of steatorrhœa with the highest recorded values. Published cases show that in this syndrome gastrointestinal symptoms are the rule; diarrhœa is common, and hypertrophic gastritis has been demonstrated 6 times and jejunitis once. In 1 case of SCHWARTZ and JARNUM gastrectomy resulted in dramatic relief; three months after operation the patient had no œdema, and the serum-albumin level and ^{131}I-P.V.P. test were normal. Examination of the diseased gut has shown in most cases that " peculiar granules ", similar to hæmofuchsin, are present in the cells of the external muscle layer. A similar observation has been made in sprue.[10]

Fascinating possibilities now present themselves. Clearly serum-albumin may pass into the gut and be lost to the body owing to disease of the stomach or small or large intestine. Is this a primary or a secondary disorder —does the protein loss cause the hypertrophic gastritis or vice versa? Is it a primary disorder when it presents with œdema, and a secondary one when it complicates

1. Sarkar, S. N. *Nature, Lond.* 1948, **162**, 265.
2. Pearson, J. D., Veal, N., Vetter, H. *Strahlentherapie*, 1958, Sonderband 38, p. 290.
3. *Lancet*, 1958, ii, 1000.
4. Csépai, K. *Klin. Wschr.* 1923, **2**, 1988.
5. Cope, C. L., Goadby, H. K. *Lancet*, 1935, i, 1038.
6. Albright, F., Bartter, F. C., Forbes, A. P. *Trans. Ass. Amer. Phys.* 1949, **62**, 204.
7. Citrin, Y., Sterling, K., Halstead, J. A. *New Engl. J. Med.* 1957, **257**, 906.
8. Steinfeld, J. L., Davidson, J. D., Gordon, R. S., Jr. *J. clin. Invest.* 1957, **36**, 931.
9. Gordon, R. S., Jr. *J. Polym. Sci.* 1958, **31**, 191.
10. Ehrenbut, W. *Z. Kinderheilk.* 1954, **74**, 141.

ulcerative colitis? What is the mechanism of the protein loss—is it comparable to exudation or transudation? What is the nature of the granules seen in the muscles? Do these new findings have any bearing on the known discrepancy between appetite and fatness? These and many other questions urgently await answers, and the tool for their study is ready to hand.

There remains a problem in semantics. What should this disease process be called? Clearly it is surrounded by two many unsolved problems for us to suggest a final name; and an interim one should be descriptive, non-committal, and brief. A new term, analogous to proteinuria, is needed. Perhaps "protein-losing gastroenteropathy" would suffice for the moment.

The Welfare of Children in Hospital

FEW if any countries with a standard of living similar to ours have spent so little on hospital building in the past twenty years, and yet given so much thought to the welfare of children in hospital; and no country in the world has such a high standard of medicine with such poor hospital buildings. Possibly our hospital buildings are so appallingly out of date, and the prospect of replacing them in our lifetime is so small, that the tantalising sight of massive office blocks springing up in our large cities makes us concentrate on doing our best to make children happy in existing accommodation. The amount of thought given in this country to the welfare of children in hospital is well exemplified by an excellent report [1] by a committee appointed by the Central Health Services Council in 1956, under the chairmanship of Sir HARRY PLATT.

The report opens with a note about the extent of the problem. On the night of the 1951 Census 36,856 children aged 4 weeks to 14 years were in hospital in England and Wales. In 1955 about 685,000 children under 15 were admitted to non-mental hospitals. In four six-week periods in 1956–57, of 17,830 children under 16 who were admitted to hospitals in fourteen selected groups, 30% were admitted to adult wards. The committee points to the need for avoiding admission of children to hospital where possible, and the importance of not admitting children to adult wards. It calls also for unrestricted visiting, as opposed to mere daily visiting; the provision of amenities for visitors (especially in long-stay hospitals), including a canteen and a playroom for siblings; and the abolition of restrictions on visiting in infectious-disease hospitals, and of the out-of-date practice of only allowing visitors to look through a glass window at the child. The committee rightly deprecates the use of cubicles, except where essential. (It might have added that isolation in single rooms is a grave disadvantage of admitting a child to a nursing-home or private block of a hospital.) Children are far happier in a ward with other children; and, so far as possible, children should be grouped together according to their ages. If a child has to be admitted a second time he should enter the same ward as before, so that he will know some of the nurses and doctors.

The report refers to the importance of the first impression. Many hospital authorities might profitably give thought to this. In how many admission departments are the parents and child kept waiting in a dark draughty corridor, sitting on a wood bench, often for quite a long time, until eventually a house-surgeon or house-physician can be found to take the history and decide to which ward the child should go? Could not children whose admission has been arranged by telephone be sent straight up to the ward (preferably the playroom), instead of being kept waiting in the casualty department?

The committee mentions the need for attention to the child's toilet needs in hospital—a point to which Prof. R. S. ILLINGWORTH [2] has lately referred. It is well known that bedwetting develops in some children after discharge from hospital. This may sometimes be due, not to emotional trauma, but to the failure of the nurses—often because of pressure of work and staff shortages—to attend regularly to the child's needs. A child in a cubicle cannot easily make these known: there is no bell which he can ring, even if he were old enough. The young child, who has recently acquired control of the bladder, has considerable urgency, and once he feels the need to empty the bladder, he cannot wait. It is altogether too easy in a hospital to have soiled linen washed.

Although the report rightly says that separate children's hospitals cannot reasonably be provided everywhere, because visiting is difficult or impossible if parents have to travel too far daily, it does not mention the desirability of having separate children's hospitals where the population is large enough for these to be economically and geographically reasonable. The standard of pædiatric care is ordinarily higher in such hospitals than in a children's department of a general hospital, unless this department is so large as to be virtually a children's hospital itself. Closure of a well-equipped children's hospital for administrative convenience cannot be excused on the ground that beds for the children can be found in smaller units elsewhere. As Mr. DENIS BROWNE remarks on p. 358, beds differ. To close or contract a good children's hospital at a time when so many children are being looked after in unsuitable beds—often in adult wards—is to accept a heavy responsibility.

The report mentions visiting in infectious-disease units, but does not emphasise the need for every children's hospital and general hospital to have its own isolation unit. Surely it is anachronistic to transfer children from a well-equipped children's hospital, with a full team and complete laboratory resources, to an infectious-disease hospital with no pædiatrician, no educational arrangements, and inadequate or non-existent laboratory facilities? Acute gastroenteritis, a highly dangerous disease of infancy, should, we suggest, be treated in an isolation unit of a children's hospital, where there are all the necessary facilities.

1. Ministry of Health: Central Health Services Council. The Welfare of Children in Hospital: report of the committee. H.M. Stationery Office. Pp. 42. 2s. 6d.

2. Illingworth, R. S. *Lancet*, 1958, ii, 165.

The committee speaks of the desirability of not putting a child to bed, if this can be avoided, as soon as he is admitted to a ward. Furthermore, as ILLINGWORTH has pointed out, the medical staff should make a conscious effort to get children up as soon as possible. Very few medical conditions necessitate an afebrile, or nearly afebrile, child staying in bed. What harm is done by letting these children sit up in chairs and play? Doctors should continually ask themselves on a ward round why each child should be in bed instead of being allowed up. In the same way doctors in hospital should ask themselves at each bed what exactly is being gained by keeping the child in hospital. Could the duration of stay in some long-stay hospitals be reduced? We now know that primary tuberculosis in children need no longer be nursed in such hospitals, unless there are special social difficulties at home. The children do just as well at home. And what about some other long-stay patients? With proper use of home-nursing schemes and with home helps, could not some of them be looked after at home?

There is room for experimentation in the care of children in hospital. For instance, can fretting in children separated from their parents be reduced, and the work of the night staff correspondingly eased, by letting many of them go home for the night? We do not know whether this would work; the daily return to hospital might cause more trauma than the daily return home prevents. But at least many children in hospital could be allowed out for meals, for a short visit to their home, or to the nearby park.

Will the day come when a brother or sister will occasionally be allowed to visit? And will the day come when a child will be occasionally allowed to visit his sick parent in hospital?

Annotations

INFLUENZA AGAIN

THERE are many reports of influenza at the moment, but the situation is nevertheless very different from that last winter. Then we had an epidemic with high morbidity arising as part of the world-wide spread of the new Asian influenza virus A. The epidemic reached its peak in this country in October, 1957, but then dragged on throughout the winter. This winter influenza appeared first in December, but until now it does not seem to have spread widely in the population. Localised outbreaks in places far apart and epidemics in schools—especially boarding-schools—have been the pattern. Reported deaths from influenza in England and Wales during the past few weeks are five to ten times fewer than those of a year ago. Laboratory reports mention the recovery of influenza virus B from some cases, but Asian virus has also been isolated this winter.

So far there has been little news of epidemic influenza from abroad. Scattered outbreaks due to influenza virus B have been reported from Holland and Italy, and outbreaks have also occurred in Russia; but there is no sign of a recrudescence of last year's epidemic. The pattern of scattered outbreaks affecting particularly schools and residential communities is characteristic of influenza-B infection; and it seems likely that the Asian virus produced sufficient herd immunity last year to prevent the appearance of a widespread epidemic at the moment.

If influenza virus B is the main culprit this year it will be interesting to see whether a single antigenic strain is responsible for outbreaks in different countries. Also, any Asian viruses isolated will be worth watching for antigenic changes from last year. But if the past behaviour of these viruses is any guide, major antigenic changes are unlikely to develop for a few years, and we may have to wait two or three years for the next big influenza-A epidemic. Those who remember crowded waiting-rooms last year will bear this interval without undue impatience.

SPUTNIKS AND BIOLOGICAL SCIENCES

ON the occasion of the twenty-first Party Congress, the Russian *Bulletin of Experimental Biology and Medicine* has surveyed recent work and prospects in Russian science.[1] In this nobody will grudge our Russian colleagues a certain tone of satisfaction; and if their medical and biological wing can keep up with the artificial satellites and nuclear-powered icebreakers they will have grounds for still more. The medical and biological programme described here is a hard-headed one, with no evidence of a competitive bias towards the spectacular. It recognises that the chief achievement of Russian post-revolutionary medicine has been in straightforward public health, in the provision of health services and their reconstruction after they were destroyed by war—an undertaking which rates several sputniks. In original research, the chief credits are claimed (though single discoveries are not enumerated) for pavlovian "nervism" and its clinical application, particularly in developmental physiopathology; for pharmacological research on spasmolytic and curariform drugs, antibiotics, and hormones; for biochemical work on protein metabolism and structure; and for bacteriological studies, especially on the use of bacteria and moulds as synthetic agents, and on transformation. A large amount of work is also going into the immunological study of cancer and of the homograft reaction, and into the comparative study of regeneration processes—the writer underlines that this topic should be approached "not simply from the angle of general biology, but first and foremost in its medical aspect". Embryology is recognised as a discipline in its own right, involving a combined physiological, biochemical, and immunological attack on the problem of cell and tissue differentiation—again with emphasis on applications. This, like the immunology of cancer, is a characteristic interest of Russian biologists, going back to the school of Metchnikov.

On the status of genetics, the writer says:

"Discussions in the field of genetics have provoked much interest in somatic cell mutation, which opens the possibility of using genetic data to study the mechanism of malignant growth, and has thrown some light on problems of tissue grafting. At the same time, there has been a noticeable lagging in research on the influence of heredity in various diseases. The wide use of atomic energy has stimulated the growth of radiation genetics, and places new tasks before Soviet biologists and medical men."

The survey does not mention either Michurinism or the theory of cellular neoformation which was agitating Russian biology two or three years ago. Of the projects for the future, the most interesting seems likely to be a

1. *Bull. exp. Biol. Med., Mosc.* 1958, **46**, no. 12, p. 1.

large-scale move into gerontology. This too has always attracted Russian workers, and it will be interesting to see how it is to be approached—the subject almost certainly cannot be "sputniked". The keenness, always present in Russian pronouncements, to concentrate on immediate application in man is without doubt humane in intention. It might work here; but perhaps the greatest contribution of the sputniks to Russian science will prove to be the removal of any pressure to achieve parity through the spectacular—a hazard to which research on ageing is particularly vulnerable.

The survey does not give many figures; but one comment of interest is that the mean expectation of life based on the 1955–56 life table was "more than twice that in prerevolutionary times"—for 1954–55 it was apparently 61 years at birth for men and 67 for women,[2] which agrees well with this. This is about the same as that for Austria and a little less than that for Northern Ireland. If the mean covers the full climatic and ethnic diversity of the U.S.S.R. it represents a very satisfactory medical achievement.

LEUCOTOMY FOR PAIN

FRONTAL leucotomy has been used in the treatment of intractable pain for over a decade. It was originally reasoned that, if leucotomy reduced anxiety about expected future events, then it might do the same for expected recurrence of pain. By and large this was proved to be the case. One consequence unforeseen, though certainly foreseeable from the uninhibited conduct of leucotomy patients, was that when pain came the immediate reaction was even brisker than before operation, although apprehension of the next bout was absent. The procedure was applied largely as a last resort in patients with incurable lesions, and no attempt was made to establish any special indications for operating. This application of leucotomy is now declining. By contrast its use where persistent pain follows some minor organic lesion and is accompanied by distinct psychiatric symptoms is increasing.

Elithorn et al.[3] made a retrospective study of 25 patients who had leucotomies primarily for persistent pain. All had an organic lesion which could be regarded as playing some causal part; and all had a psychiatric reaction as well. In assessing results they obtained reports from patients, relatives, and the group of physicians responsible for the operation, and in addition devised a scale of social efficiency by which the preoperative and postoperative states were compared.

Their findings are interesting. Only 5 patients showed improvement in pain, and in only 2 of these was it considered much improved. But 8 patients thought the operation had helped; and 8 relatives also thought this, though only 5 of these agreed with the patient's own assessment. The physicians judged that 17 of the patients were improved or greatly improved. On the social-rating scale, 20 patients showed evidence of improvement and in 10 this was considerable. Of the 8 cases assessed as unimproved or worse by the physicians, 6 had pain rated very severe or severe and of organic origin. It seems that severe pain due to an organic lesion is unlikely to be benefited. On the other hand, general disability may sometimes be considerably reduced without much specific relief of pain, owing to improvement in the psychiatric reaction—depression and anxiety apparently responding best. In the past leucotomy in the treatment of such patients has been regarded as a counsel of despair. Elithorn et al. have provided some much-needed information for a more rational therapeutic approach.

2. *Popul. Index*, 1958, **24**, 395.
3. Elithorn, A., Glithero, E., Slater, E. *J. Neurol. Neurosurg. Psychiat.* 1958, **21**, 249.

OBSTETRIC CARE OF THE TUBERCULOUS PATIENT

THE prevalence of tuberculosis in pregnant women is not precisely known; the recorded figures vary with the intensity of the diagnostic efforts. Correlation of history and clinical evidence may reveal 1 patient with active tuberculosis in 200 attending antenatal clinics, whereas routine radiological screening may show a significant chest lesion in three times this number. It is estimated that over 30,000 pregnant tuberculous women are delivered annually in the U.S.A.[1] The Joint Tuberculosis Council has now published the report of a committee [2] which has reviewed the position.

Eight questions relevant to patient care were considered, and the answers afford a useful guide to practitioners and at the same time emphasise the change in outlook due to modern therapy. Tuberculosis can be cured or controlled without the therapeutic agents used affecting the fœtus adversely. Lung resection or thoracoplasty can be performed during the first twenty-four weeks without disturbing the pregnancy, but surgery is now seldom necessary. Pneumoperitoneum is contraindicated. Clinical reassessment is essential during pregnancy and the puerperium.

Three of the eight questions dealt with the controversial subject of antenatal radiography. Tomography and screening, says the report, should be avoided or deferred until the puerperium; but routine antenatal chest X-rays, kept to the minimum essential for accurate diagnosis, are recommended in the interests of both mother and babe. The radiographs should be taken at about the thirteenth week, and not later than the twenty-sixth week unless urgently required. The report suggests that routine tuberculin-testing in antenatal clinics could reduce the number of radiographic examinations needed. Somatic maternal damage is not a danger with properly controlled chest radiography; but ovarian dosage, though minute, is inevitable owing to scatter and adds to the population-gonad dose. There is possibly a slight risk of fœtal somatic damage in the first twelve weeks of pregnancy, although the danger can be reduced to a minimum by careful technique; but, the report adds, radiation of the fœtal gonads with its inherent risks to future generations may be a serious problem.

Pregnant women with active lesions should be nursed in a sanatorium or a chest unit in a general hospital, and delivered in an obstetric unit with isolation facilities. Good liaison between the physician, obstetrician, and pædiatrician is essential. Breast-feeding may be allowed when a mother who is non-infective is anxious to nurse her baby, but the infant should be vaccinated with B.C.G. If the mother has an active lesion the infant should be separated at birth, vaccinated, and segregated until after Mantoux conversion. Segregation may be difficult or impossible to arrange under certain conditions, in which case the infant should be given isoniazid 3–5 mg. per lb. body-weight daily while it stays with the mother. When satisfactory arrangements have been made the isoniazid is discontinued and B.C.G. vaccination given; the infant is not returned to the mother until after Mantoux

1. Schaefer, G. Tuberculosis in Obstetrics and Gynæcology. London, 1956.
2. Joint Tuberculosis Council: Report of the Joint Pædiatric and Obstetric Committee on the Antenatal and Obstetric Care of Tuberculous Patients and Measures to Safeguard their Infants. Obtainable from the Hon. Secretary, Hawkmoor Chest Hospital, Bovey Tracey, Devon. 3*d*.

conversion. The report remarks that an effective isoniazid-resistant B.C.G. vaccine may become generally available, in which event segregation would not be necessary; the infant would be vaccinated at birth and receive isoniazid concurrently until Mantoux conversion has taken place.

COLD INJURY

ALMOST a century and a half ago Baron Larrey, surgeon to the French armies in the Napoleonic wars, gave a classic clinical description of cold injuries. This is reproduced by Whayne and DeBakey [1] in their detailed review of such injuries in the 1939–45 war, which clearly underlines the uncertainty of the pathogenesis and the difficulties of management—though the Korean campaign, with which these authors are not concerned, added a good deal to our knowledge.

How cold injures the tissues is not entirely clear. Tissue anoxia, due simply to vasoconstriction, is generally regarded as the main factor in the cold phase; and if the ambient temperature is relatively high, as it often is in trench-foot, metabolism may be proceeding at a significant rate with obviously untoward consequences. Re-warming results in outpouring of plasma with resultant intravascular stasis or even thrombosis. The extent of this occlusion seems to be the most important factor in deciding tissue loss; but Friedman,[2] on the basis of histological studies at the American Army Institute of Pathology, suggested that there may possibly be a direct thermal effect on structures rich in lipoids (e.g., adipose tissues and myelinated nerve-fibres). Abnormal metabolites accumulating in the period of reversible anoxia may also play some part. The crystallisation of tissue-fluids in frostbite almost certainly causes little, if any, permanent damage.

The treatment of cold injury is no less undecided than its pathogenesis. There has been much argument as to whether the affected part should be warmed or not, and if so, how quickly it should be warmed. The efficacy of rapid re-warming, first advocated by Ariev,[3] has been proved in animals, though not in man; and, if anoxia is assumed to be the prime enemy, it seems logical to adopt this method. Gentleness is important, and therefore such methods of restoring the circulation as rubbing with snow are contraindicated. After re-warming, the affected limbs should be elevated and exposed to the air at a temperature of about 70°F. General body warmth should be maintained and sleep encouraged. Early physiotherapy is essential. Anticoagulants might reasonably be expected to be of value in preventing thrombosis; but experience with their use in Korea was disappointing. The management of blisters, infection, and gangrene follows accepted surgical principles. The attitude towards amputation, which is only rarely needed, should be particularly conservative. Emergency amputations are never indicated except for serious infection. Skin grafts will usually take after excision of clearly demarcated necrotic superficial tissue.

Whayne and DeBakey emphasise that sequelæ are common. The most usual ones are tenderness (particularly in the soles of the feet), paræsthesiæ, and such manifestations of excessive sympathetic activity as hyperhidrosis and cold sensitivity. They state that sympathectomy is often of real value where there is proof of such overactivity, but that there is no evidence of its usefulness in the early treatment of cold injury. Identical conclusions were reached by American and British surgeons in Korea.

The importance of acclimatisation in preventing cold injuries is evident from the example of aboriginal peoples who live naked and with little shelter in temperatures that sometimes approach freezing-point.[4] But study of the Eskimo (among whom frost injuries are reputedly extremely rare [5]) has shown that other factors, including clothing, diet, and exercise, play an important part. Because not only habituation but also study and skill are needed for learning to live in extreme cold, Rodahl [6] suggests that this process should be termed "cultivation" rather than "acclimatisation".

HEPATIC AMŒBIASIS

Lamont and Pooler,[7] working in Durban, have studied 250 cases of hepatic amœbiasis and reached conclusions some of which are slightly at variance with current opinion. They suggest that no clear-cut distinction between "amœbic hepatitis" and amœbic abscess of the liver is warranted; these two differ only in degree. In other words, hepatitis is the pathological precursor of abscess. This view has been expressed by others; but it is common knowledge that, even in the absence of specific treatment, classical "amœbic hepatitis" does not invariably lead to liver abscess. From the pathological standpoint there appears to be little solid ground for the recognition of "amœbic hepatitis". The best definition of this state is that by Kean [8]: an enlarged, tender liver associated with fever, response to antiamœbic treatment, moderate leucocytosis, and a history of intestinal amœbiasis.

The Durban workers say that enlargement of the liver suggests one or more of the following lesions: (1) a localised expansive lesion within the substance of the liver; (2) a diffuse increase in the mass of either parenchyma or stroma, or both; (3) prolonged biliary obstruction with diffuse dilatation of the bile-ducts; (4) engorgement of the vascular channels, with or without œdema of the liver cells or stroma. The liver may be enlarged upwards or downwards, but also—which is not generally recognised—on a horizontal plane as well. The earliest phase of an amœbic abscess, they believe, is a "silent" focal lesion, which may either resolve without abscess formation or progress acutely or gradually. Vascular, as well as immunological, factors may be important in determining the ultimate course of hepatic reactions. They suggest that helminthiasis, which is highly prevalent in Africans in Durban, may predispose to hepatic amœbiasis, facilitating the entry of *Entamœba histolytica* into the portal circulation.

Ochsner and DeBakey [9] reported that abscesses may disappear completely on emetine therapy alone, and with this conclusion Lamont and Pooler agree. There was a prompt and striking response to specific therapy consisting of a ten-day course of emetine injections (gr. 1 daily) together with, or followed by, a three-week course of chloroquine diphosphate (1 g. for two days, followed by 0·5 g. daily). In view of the fact that the series included many "advanced cases" the death-rate (6·4%) was surprisingly low.

1. Whayne, T. F., DeBakey, M. E. *in* Cold Injury, Ground Type. Editor-in-chief: Colonel John Boyd Coates, Jr. Washington, D.C.: Government Printing Office. 1958. Pp. 570. $6.25.
2. Friedman, N. B. *Amer. J. Path.* 1945, **21**, 387.
3. Ariev, T. V. Fundamental Outlines of Present Day Knowledge of Frost Bite. Moscow, 1943.
4. Irving, L. *in* Cold Injury: transactions of the Fifth Conference, March 10–15, 1957. Edited by M. Irené Ferrer, M.D. New York: Josiah Macy, Jr., Foundation. 1958. Pp. 341. $5.95.
5. Rodahl, K. *ibid.* p. 17.
6. Rodahl, K. *ibid.* p. 197.
7. Lamont, N. McE., Pooler, N. R. *Quart. J. Med.* 1958, **27**, 389.
8. Kean, B. H. *A.M.A. Arch. intern. Med.* 1955, **96**, 667.
9. Ochsner, A., DeBakey, M. *Surgery*, 1943, **13**, 460, 612.

Special Articles

SENSITIVITY OF CLINICALLY IMPORTANT BACTERIA TO SIX COMMON ANTIBACTERIAL SUBSTANCES

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THE frequent use of antibiotics without laboratory control suggested to us that it might be of interest to record the sensitivity of organisms isolated in this laboratory in 1956–57, to analyse the sites of origin of these organisms in relation to their sensitivities, and to compare the sensitivities of organisms isolated from inpatients and others. Such an analysis should show whether there was a significant trend towards the development of resistance to antibiotics among the various bacterial genera.

Several sensitivity analyses have been reported in the U.S.A. and a few in this country (Fairbrother et al. 1951, Needham and Nichols 1953, Giles and Shuttleworth 1958). These suggest that considerable variation in sensitivities is likely, not only between different geographical areas but in the same geographical area at different times. We feel, therefore, that our own results are subject to a bias even though St. Helier Hospital is a general hospital serving a large area.

TABLE II—SITES OF ORIGIN AND SENSITIVITIES OF 4780 ORGANISMS ISOLATED IN 1956–57

—	Site of origin										
	Nose	Throat	Sputum	Skin	Eye	Ear	Genito-urinary	Faeces	Blood	C.S.F.	Unknown
No. of organisms	227	280	671	104	246	194	1725	200	61	15	1057
% of organisms sensitive to:											
Penicillin	38	76	40	32	39	33	5	2	25	60	26
Streptomycin	70	37	51	71	61	60	48	60	49	47	52
Sulphonamide	65	60	67	58	67	60	50	47	48	73	52
Chloramphenicol	88	95	89	78	86	66	60	71	85	93	79
Tetracycline	79	85	72	76	75	57	38	55	72	87	58
Erythromycin	89	86	70	93	94	58	24	23	66	60	75
% of organisms recovered from each site:											
Staphylococci	69	21	22	84	64	36	10	24	51	7	62
Pneumococci	9	11	25	..	9	4	..	..	..	33	1
Streptococcus group A	3	35	1	1	1	8	0	..	3	7	3
Str. faecalis	..	1	1	3	..	4	13	..	2	..	4
Other streptococci	2	17	7	6	9	..	1	..	8	..	4
Haemophilus	6	2	18	..	2	3	..	..	..	27	0
Esch. coli	2	4	3	1	5	2	35	7	2	..	8
Aerobacter + Friedländer	2	2	7	1	..	4	7	0	13	..	3
Coliform	1	1	2	..	..	1	5	1	4	..	1
Proteus	1	1	5	..	1	20	15	18	3	..	6
Salmonella	..	..	..	..	..	..	0	14	2	..	..
Ps. aeruginosa	1	1	3	5	1	10	12	18	3	..	5
Neisseria	1	1	5	..	..	1	..	..	2	13	0
Others	2	2	2	..	7	7	2	2	5	13	2

TABLE III—COMPARISON OF SENSITIVITIES OF 2340 ORGANISMS OBTAINED FROM PATIENTS IN HOSPITAL WITH 574 FROM OTHER SOURCES (OUTPATIENT DEPARTMENT, CASUALTY, AND GENERAL PRACTICE)

—	Staphylococci		Pneumococci		*Str. faecalis*		*Haemophilus*		*Esch. coli*		*Proteus*		*Ps. aeruginosa*	
	Inpatients	Others	Inpatients	Others	Inpatients	Others	Inpatients	Others	Inpatients	Others	Inpatients	Others	Inpatients	Others
Total	856	290	155	38	208	32	106	27	510	85	287	63	218	39
% sensitive to:														
Penicillin	20	46	98	97	13	9	7	4	0	0	0	0	0	0
Streptomycin	50	82	12	13	7	3	94	92	80	85	61	63	4	6
Sulphonamide	48	71	84	94	12	15	79	78	67	81	49	62	31	28
Chloramphenicol	84	86	99	100	65	57	100	100	68	69	48	43	5	5
Tetracycline	70	86	98	97	47	54	83	92	54	60	13	15	1	5
Erythromycin	97	98	99	100	84	75	54	43	1	4	1	0	1	2

Methods and Materials

Organisms isolated from primary plate culture were subjected to sensitivity tests by the application of 5 mm. wide strips of filterpaper soaked in solutions of the various antibacterial substances and placed at right-angles to streaks of the organisms on a blood-agar plate. In the case of the sulphonamide sensitivities the blood-agar was *p*-aminobenzoic-acid-free. The spread of proteus was prevented by incorporating chloral hydrate (0·06%) in the agar.

The concentrations of the antibacterial substances used were:

Sodium penicillin	20 units per ml.
Streptomycin sulphate	400 μg. base per ml.
Sodium sulphadiazine	5% solution
Chloramphenicol	400 μg. per ml.
Tetracycline hydrochloride	400 μg. base per ml.
Erythromycin lactobionate	50 μg. base per ml.

The sensitivity tests were read after 20 hours' incubation at 37°C.

Organisms which were thought to be associated with a pathological state were subjected to sensitivity tests when requested by the clinician, but rarely otherwise. Thus not all organisms isolated during the period of the analysis are included in the results.

Details of the investigation were recorded on punch cards. All sensitivity tests in 1956 have been included, and, in addition, organisms isolated in the first two months and the last two months of 1957 have been analysed separately. Certain genera, such as *Corynebacterium* and *Clostridium*, are not included in the separate statistical analyses because too few were obtained. These are grouped under the heading of "other organisms". In addition many of the laboratory request forms gave inadequate details for correct interpretation of the site of origin of the specimen, and these are grouped under the heading "unknown".

Results

The results are recorded in tables I-IV.

TABLE I—SENSITIVITY OF 4860 ORGANISMS ISOLATED IN 1956–57

—	Staphylococci	Pneumococci	Streptococcus group A	*Str. faecalis*	Other streptococci	*Haemophilus*	*Salmonella*	*Sh. somei*	*Neisseria*	*Esch. coli*	Aerobacter (and Friedländer)	Coliform	*Proteus*	*Ps. aeruginosa*	Others
Total	1631	269	168	293	204	167	31	25	41	772	210	126	450	358	115
% sensitive to:															
Penicillin	26	99	98	11	77	5	0	0	98	0	0	1	0	0	37
Streptomycin	58	12	7	6	30	94	55	84	98	82	63	59	64	4	65
Sulphonamide	52	82	45	12	58	78	55	36	83	76	68	55	51	28	80
Chloramphenicol	86	100	98	69	93	100	81	92	100	74	63	57	51	6	83
Tetracycline	73	98	98	48	88	86	48	76	98	58	58	53	16	2	77
Erythromycin	97	99	98	83	90	60	0	0	98	1	6	9	0	1	59

TABLE IV—COMPARISON OF ANTIBIOTIC RESISTANCE OF STAPHYLOCOCCI DERIVED FROM DIFFERENT LOCALITIES AT DIFFERENT TIMES

	1956		Early 1957		Late 1957	
	Inpatients	Others	Inpatients	Others	Inpatients	Others
Total	856	290	106	53	245	81
% *sensitive to:*						
Penicillin	20	46	16	36	19	44
Streptomycin	50	82	46	87	47	79
Sulphonamide	48	71	42	67	40	62
Chloramphenicol	84	86	90	94	90	90
Tetracycline	70	86	67	75	69	82
Erythromycin	97	98	95	100	95	98
% *resistant to:*						
Penicillin and streptomycin	52	12	51	13	53	20
Penicillin, streptomycin, and sulphonamide	40	8	43	11	48	19

Discussion

Of the six antibacterial substances penicillin had the narrowest spectrum closely followed by erythromycin, although this antibiotic was frequently effective against *Hæmophilus influenzæ*. The antibacterial spectra of the other substances were wider, with a greater proportion of the individual strains within the various genera sensitive to chloramphenicol. Tetracycline was seldom active against members of the *Proteus* genus, and sulphonamides were the most effective against *Pseudomonas aeruginosa*.

The high proportion of staphylococci isolated from nasal swabs is likely to have been due to a high carrier-rate rather than to the frequency of nasal disease, but it is difficult for the bacteriologist to distinguish one state from the other in the laboratory. The reports on bacterial flora of sputum may be somewhat misleading since *Streptococcus viridans* and *Neisseria*, both of which were frequently present, were seldom reported even though they may sometimes have been important as secondary invaders. In addition it seems probable that many of the staphylococci isolated from eye swabs were not causing infection but were merely commensals; and probably the proportion of cases in which staphylococci were isolated from blood-cultures was related rather to the frequency with which this organism contaminates blood-cultures than to bacteræmia. Finally, we believe that the high prevalence of *Ps. aeruginosa* in the urine of gynæcology patients was related to the use of wooden spigots in catheters postoperatively—a practice which has been discontinued.

The comparison of the sensitivities of organisms isolated from inpatients and from other sources shows no statistically significant difference between the bacterial genera apart from the staphylococci. The figures of 20% of inpatient staphylococci sensitive to penicillin, compared with 46% of the staphylococci isolated from other sources, is highly significant ($P=0.001$). The figures for streptomycin and sulphonamide are even more significant.

Comparison of the sensitivities of staphylococci isolated during 1957 with the findings in 1956 shows a definite increase in antibiotic resistance with time. When the antibiotic sensitivities were grouped to eliminate individual non-significant alterations in sensitivity, it was found that 40% of the staphylococci isolated in 1956 were resistant to penicillin, streptomycin, and sulphonamide compared with 48% of the staphylococci isolated during the last six weeks of 1957 ($P=0.02$). Staphylococci isolated from patients outside the hospital were resistant to penicillin, streptomycin, and sulphonamide in 8% of cases, while staphylococci from inpatients showed this resistance in 40% of cases. This suggests that at least 274 patients became infected with staphylococci in the hospital in 1956.

TABLE V—RESISTANCE OF STAPHYLOCOCCI TO EACH OF FIVE ANTIBIOTICS COMPARED WITH THE AMOUNT OF EACH ANTIBIOTIC USED IN THE HOSPITAL

Antibiotic	% resistant inpatient staphylococci (April, 1957)	Amount used between April, 1956, and April, 1957
Penicillin	84	54,000 mega units
Streptomycin	54	38,390 g.
Tetracycline	33	7395 g.
Chloramphenicol	10	3750 g.
Erythromycin	5	1177 g.

In the year April, 1956, to April, 1957, dispensary returns showed that £10,002 was spent on antibiotics (sulphonamides excluded). Table v shows a breakdown of these returns. No dogmatic conclusions can be drawn from the figures in this table. Nevertheless, the overall impression is that the resistance of staphylococci to antibiotics is related to the extent to which these antibiotics are used.

Summary

The sensitivities of bacteria to six widely used antibacterial drugs in 1956–57 are analysed.

The resistance of staphylococci to an antibiotic seems to be related to the amount of the antibiotic used.

We are grateful to Messrs. Parke, Davis & Company, Ltd., for supply of punch cards which greatly facilitated the analysis.

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DIRECTOR-GENERAL, N.H.S.?

Concluding a lecture to the Royal Society of Edinburgh on Jan. 12, Prof. W. L. M. Perry said:

The organisation of the public health services—in their widest sense—in this country is, to my mind, no longer adequate. The Civil Service pattern of departmental administration was a highly satisfactory solution to the problems of the 19th century and even of the first two decades of this century. An intelligent man with a liberal education who joined the senior Civil Service could be posted to any Ministry and could confidently set about acquiring the necessary knowledge of the particular technology involved. Seldom would this take him longer than a year. Thereafter he was well equipped to make decisions, advised from time to time by technical experts.

The position has changed out of all recognition. Policy is probably best made by laymen; but the politician with a small staff can accomplish this. The executive functions of the Ministry of Health are so complicated, and so highly technical, that the place of the senior Civil Servant as the primary cog of the machine is completely inappropriate. I suggest that the example of another new technology be followed, and that the running of the health services be put in the hands of the director-general of an agency—as is the case with Atomic Energy. I believe that the responsibility for the public health administration should be in the hands of people trained in public health and that they should be charged with the carrying out of the policy decided by the Minister. The director-general should be given both power and responsibility and should be judged by his performance. I believe that this change would mean a great improvement in the ease with which men of the right training and calibre would be recruited to the service; and I firmly believe that only in this way can vision and long-sightedness be introduced into the planning of the public health services, and of preventive medicine.

Reconstruction

"ANOTHER PLACE"

DENIS BROWNE
F.R.C.S.

LAST week I attended for the first time a debate in the House of Lords. On the other side of the river there was a sight closely connected with the subject of that debate . . . the bombed and ruined eastern third of one of the most famous hospitals in Europe, St. Thomas's. Why these ruins remain some fourteen years after the end of the latest German war it is not easy to understand. It cannot be because we are not able at present to build: all along the river huge new blocks are arising. It is not because the wards are not needed; the long lists of patients waiting for urgently necessary admission prove the contrary. Surely it would win votes to show that those in power were concerned with the state of the poor; and as to extravagance, this is the age of spending hundreds of millions on the Conquest of Emptiness, and in ten years time the cost of rebuilding will be several times what it is today.

Whatever the cause of the almost complete stopping of hospital building in Britain since the start of the Health Service, it is a fact, and it is having very unfortunate results. One of them is a scramble for any decent buildings that exist; and the debate was to be about the taking away of Princess Louise Hospital from the children for whom it was quite recently built, for the use of adult patients.

The debate started with a rather upsetting bit of business, not without bearing on what followed. A very gallant airman, Lord DOWDING, raised the question of the deaths of a few hundred monkeys on their way through London to be sacrificed in the cause of science and the survival of more advanced types. Replying for the Establishment, Lord CHESHAM, like the Staff Officer who so annoyed Hotspur, obviously thought it unmannerly that these slovenly unhandsome little corpses should be brought betwixt the wind and his nobility. Lord Dowding was seen off with the answers that the regulations had all been observed, and that the responsibility was not ours since the animals were merely in transit; and we passed by on the other side.

Then Lord BALFOUR OF BURLEIGH rose to attempt to save the Princess Louise Hospital for Children, whose building by local subscription he had done much to arrange. At the beginning of the Health Service it had sought refuge with the teaching hospital of St. Mary's from subjection to the local authorities—on the strength of a definite promise that it would be kept as a children's hospital and used as part of St. Mary's pædiatric unit. The Minister of Health had, however, agreed to let the teaching hospital take over half its beds for obstetrical cases, in what everyone concerned believed to be a first bite.

Lord Balfour began by setting out facts of common knowledge, which unfortunately nearly every speaker in the five hours' debate found it necessary to state again. These were that the pattern of disease is changing, leaving the country with too many children's beds and too few for adults; so that adjustments between the two needed to be made. The accommodation for children was very variable, running from specially built, staffed, and equipped hospitals, like the one under discussion, through wards in teaching hospitals, wards in large efficient hospitals, and wards in small inefficient hospitals, down to the universally condemned use of adult beds and the admission of non-infective children to Fever Hospitals.

A recent report of a special committee of the Royal College of Physicians had classified accommodation in the order of desirability just given, so that it was necessary for the opponents of the hospital, when their turn came, to establish that this report did not mean what it very clearly said.

After quoting figures to show that the work of the Princess Louise was steadily increasing, Lord Balfour made the not unreasonable suggestion that, as children's wards had to be closed, the less efficient should be closed before the efficient. Here he was on dangerous ground, for it would have been fatal to give a chance to the opposition of accusing him of insulting any group of hospitals and their staff. Nothing was more curious in the subsequent debate than the complete lack of any inquiry as to how children were to get the best treatment. The nearest approach to it was an admission that, though all children's wards were equal, those of a hospital of the type put first by the Royal College of Physicians, such as Great Ormond Street, were more equal than the others.

The Minister in announcing his intention had put it in official prose: "He was convinced that it is practicable for those entitled to avail themselves of the objects of the Princess Louise Hospital for Children to enjoy similar facilities in suitable neighbouring hospitals." Miss Gertrude Stein would have put it more succinctly in another variant of the English language: "A bed is a bed is a bed."

Two other curious gaps appear: one is the absence of any attempt to get authoritative pædiatric opinion on the fate of the children, presumably because it was too obvious what this would be. The second is the lack of any summing up of the dispute from another important angle, that of business efficiency, from such an authority as that of the manager of one of the great chemical or engineering firms. Perhaps in this case also the comments might be rather incisive.

A leading article in *The Times* that morning had suggested the same obvious solution as Lord Balfour went on to put forward. This was that St. Mary's should give back a hospital which they had acquired under a repudiated promise, and which they did not want to use for its designed purpose, to the Regional Hospital Board. This proposal was, of course, the proper subject of the debate: it was not debated.

Lord MORAN then rose to speak for the Establishment; perhaps the most powerful figure in medical politics, head and largely maker of a most successful medical school, long president of the Royal College of Physicians, known in the profession for his agility in debate and unexpectedness in action. His attack was calculated to appeal to his mainly lay audience. His first point was that a senseless outcry always arose when any attempt was made to adjust the organisation of medicine to changing conditions, and he gave several instances in which local opposition had been successfully suppressed. Neither he nor any subsequent speaker mentioned a closely similar case in which it had been successful: the saving by public outcry of Paddington Green Children's Hospital, which

was quoted later in the debate with approval as doing excellent work.

He went on to say that, before the Health Service, hospitals were dumped anywhere: "One might get two children's hospitals in the same street." This was an effective remark in a rapid speech, but it would have been more convincing if he had given even a single instance of such remarkable distribution.

He then compared this protest to a quite imaginary demand that empty tuberculosis hospitals taken over should be restored to their original purpose in obedience to "local clamour". I cannot look on this as anything but disingenuous, since no such demand has ever been, or ever will be, made. He admitted the promise about Princess Louise's future, but said it had been made by a different Board of Governors from those who now held the same positions. This quibble was too much for several noble lords who spoke later, in spite of its backing by the legal Lord Cohen. He mentioned the objection, raised later by Lord Amulree, about the dangers of bringing healthy babies into the same building as ill ones —a proposal that would horrify any pædiatrician, who knows that one mistake by a wardmaid might produce a miniature version of the tragedy of Lord Dowding's monkeys. This was treated in a characteristic way by Lord Moran and a subsequent speaker. The report of the Royal College of Physicians had recommended that there should be a close link between any obstetric unit and a children's unit. There is this link, for instance, between the largest obstetric unit, Queen Charlotte's, and the largest children's hospital, Great Ormond Street. But a link between two institutions several miles apart is a very different thing from having two mutually dangerous classes of patients in the same building, with merely a corridor between them.

Next came prophecy (always a chancy business) that the staff of Princess Louise at the end of two years would plead for the retention of the obstetric beds. Be that as it may, Lord Balfour rose to say that they certainly did not like the idea now.

Then came a typical bombshell. Lord Moran said that he had written to the twenty members of the committee of the Royal College of Physicians, who had produced the report in favour of special children's hospitals, asking that they should say by return of post "what was in their minds". Eighteen replied, and with one exception admitted that they had not meant what every reader of the report had taken them to mean. Instead of laying down a national policy for the treatment of children, they only had one hospital in mind—the Sheffield Children's Hospital, with 221 beds. The more I think of this statement the more odd it becomes; perhaps it would make things clearer if we knew the terms of the letter of inquiry, and heard from a few of those who answered. But as we were given nothing more by Lord Moran, and as none of the legal Lords present mentioned the laws of evidence, this very effective contribution to the debate takes its place among the mysteries of the afternoon.

From this he went on to argue that a children's hospital must be large, which prompts the obvious question as to why then he was scattering children instead of concentrating them. All through his argument ran the notion that the recent decline in children's diseases would continue till none were ill at all. In a later interjection he scoffed at the idea of using beds "in perpetuity for children when children's diseases have disappeared". This remarkable assumption is combined with pointing out the advantages of having beds for sick children in the same building as babies produced by ordinary mothers, and so available for the newborn who need them (estimated by a subsequent speaker at one in a thousand). All this in a speech accusing the other side of talking unrealistic nonsense.

It is interesting to note the objection to doing what must strike any factory manager as the obvious thing: filling up Princess Louise from the partially empty children's beds in the neighbourhood and then converting the freed wards to much-needed adult use. In a debate on the same subject some months previously Lord Moran had said that if he could have "administrative control" of the beds in surrounding hospitals which accommodated cases from St. Mary's he would have no further demands. Apparently administrative control means the power of admitting only such cases as are useful for educating medical students; and this raises the question whether a teaching hospital exists for the service of the public, or whether the public exists to supply educative material for the profession. One or two noble Lords looked like following this up, but apparently concluded it was rather too hot a subject.

Lord Moran ended with the warning that the proposal of Lord Balfour of Burleigh and *The Times* would infallibly lead to utter chaos throughout the profession, and sat down having produced an immense effect.

Lord COTTESLOE followed to deal with *The Times* by saying that they were out of date, for, though eighteen months ago their proposal would have been possible, it was now out of the question. He left as one of the many unsolved questions of the afternoon the exact nature of the changed circumstances which had caused this impossibility. Lord Cottesloe also explained that, though the 200 beds labelled for children in the immediate neighbourhood lay partially empty, this state was necessary to allow for casualties and emergencies: but as the partially empty state of Princess Louise beds was the reason given for taking them over, this again seems queer.

Lord AMULREE delivered a moderate and reasoned support of Lord Balfour of Burleigh, and various others backed him. But nothing availed against the succession of supporters of the Government reiterating Lord Balfour's setting-out of the need for change as if it were an argument against his suggestion of the way this change should be made.

Lord STONHAM gave a long account of the sufferings of a mother in labour seeking admission, but did not suggest that the conversion to maternity beds of the surplus children's beds in the area might help. To the suggestion by several speakers that this might be done, it was replied that this would involve conversion of beds and the making of labour wards. That this conversion would also be necessary at Princess Louise did not seem to strike anybody.

Towards the end of the five hours the most famous modern orator of the profession, the medical Lord Cohen, rose to support the Government. In his description of the situation Lord COHEN spoke of " unmasking Nature's mysteries " where others had merely said the statistics were improving. His peroration was much the best of many comparisons made that afternoon between the present situation of medicine and that of any army in battle. He pointed out that our strategy must be fluid

and flexible under commanding officers who have a plan. Admittedly Lord Balfour's plan was not as flexible as the average fluid, but there was no reason given as to why it would not work. However, he sat down to the Lords' version of loud applause, and it was obvious that the battle had been won and lost.

Winding up as spokesman for the Government, Lord DUNDEE made a nice change by putting the situation into Latin, but rather lost his nerve after *mutantur*; he did not proceed to the next line in the epigram from which the tag comes, to the effect that as men grow older they get worse.

Finally Lord BALFOUR OF BURLEIGH rose for his reply, and it was obvious that he had had more than enough of medical Lords and tricky arguments. Of one of the latter he said that he had never heard such nonsense in his life; and he expressed the feelings of quite a few when he suggested that the Minister of Health might knock various heads together if they persisted in going on like this.

The Establishment won handsomely in the subsequent division, and, as I left, for some reason Lord Dowding's monkeys occurred to me. Perhaps that is because one who actually works with children sees them not as figures of " bed occupancy " but as those who live or die, are crippled or sound, according to the way they are treated.

It is worth noting that the next Children's Hospital on the list for a take-over bid for its buildings is Queen Mary's, Carshalton. The argument against Princess Louise was that it was too small; the argument against Queen Mary's is that it is too large. The argument against Queen Mary's is that it is difficult to visit (it lies in a densely populated residential district): in the case of Princess Louise the argument that it was easy to visit was brushed aside as unworthy of consideration.

In neither case has there been any suggestion that the children themselves will be any better off for the change.

Parliament

Local Authorities' Mental Health Services

IN 1957–58 a total sum of £3,412,000 was brought to account by local health authorities as their net expenditure in carrying out duties under the Lunacy and Mental Treatment Acts, 1890–1930, and the Mental Deficiency Acts, 1913–1938. This represents about 93⅓% of their total net expenditure on mental health services.

The amounts spent vary. The six highest were:

£246,000, London	£124,000, Essex
£196,000, Middlesex	£118,000, West Riding of Yorkshire
£177,000, Lancashire	£109,000, Kent

The six lowest were:

£1700, Worcester	£500, Breconshire
£1200, Montgomeryshire	£300, Merionethshire
£1200, Cardiganshire	£300, Rutland

Proposed Closure of a Maternity Hospital

In an adjournment debate on Feb. 6 Mr. WILLIAM TEELING declared that the matron and staff of the Sussex Maternity Hospital had been told that the hospital was to be closed within a year or two. This maternity hospital, the oldest in England, had been founded in 1831; and to the people of Brighton and Hove its closure would be a calamity. It was proposed to provide more maternity beds at Brighton General Hospital; but mothers in the area argued that childbirth was not an illness but a natural happening which should not be linked with sickness in hospitals. The Brighton and Mid-Sussex division of the British Medical Association had described the proposal as " timid, inadequate, and uneconomic ". The division was averse to closing the hospital unless a new maternity unit was built as the initial step in creating a new hospital centre.

Mr. RICHARD THOMPSON, parliamentary secretary to the Ministry of Health, said that no decision to close the hospital had been reached. The South East Metropolitan Regional Hospital Board was holding discussions locally; but it had put no proposal to the Minister. The staff of the hospital had been informed on Jan. 2 of the proposal; but it had been made clear that this was purely a proposal, and that the position of the staff would be safeguarded.

White-paper into Bill

Last year the Government published a white-paper on provision for old age, which was discussed in the House of Commons in November.[1] On Jan. 27 Mr. JOHN BOYD-CARPENTER, the Minister of Pensions and National Insurance, moved the second reading of a Bill, which, he said, reproduced the main framework of these proposals with some important variations, including the following:

The Exchequer contribution will no longer be fixed at £170 million (though it will not be able to fall below that sum), but will be tied to a proportion of the employers' and employees' contributions.

The amount of the four quinquennial increases in the contributions can be reduced by Order, if they should not prove necessary to balance the finances of the scheme.

The increments which can be earned by men and women who work after pensionable age are improved. Twelve extra contributions will earn an increment of 1*s.* (instead of twenty-five contributions earning 1*s.* 6*d.*). This means that the maximum increment which can be earned by a single man will be 21*s.* a week (instead of 15*s.*). The weekly earnings limit for retirement pensioners and widows will be raised to 60*s.* (instead of 50*s.*) and for widowed mothers to 80*s.* (instead of 60*s.*).

1. See *Lancet*, 1958, ii, 1126.

QUESTION TIME

Long-term Hospital Patients

Mrs. EVELINE HILL asked the Minister of Pensions and National Insurance whether, in the light of the new proposals for the treatment of the mentally disordered, he would ask the National Insurance Advisory Committee to review the position under the National Insurance scheme of those patients who were detained as a result of court proceedings.—Mr. BOYD-CARPENTER: Yes. I have asked the National Insurance Advisory Committee to review the provisions of the scheme as they affect long-term hospital patients generally, including those referred to by Mrs. Hill. The following are the terms of reference:

" To review the provisions governing the liability for contributions and rights to benefit under the National Insurance scheme (not including rates of benefit or contributions) of long-term hospital patients, including mentally disordered patients ' detained in legal custody ', and patients doing work for which they receive payment; and to report."

Westminster Hospital

Lord CLITHEROE asked the Government whether it was now possible to give a date when the necessary capital money would be available to complete the Westminster Hospital's premises, thus making use of the valuable adjoining site in Page Street and enabling the hospital properly to fulfil its function as a modern teaching hospital.—The Earl of ONSLOW replied: The Minister of Health fully recognises the desirability of the proposed development at the Page Street site, to provide a proper balance for the services of Westminster Hospital. But he has not so far felt able to give this project sufficiently high priority to justify including it in his building programme in preference to other urgent and essential schemes. Many other hospitals are in even greater need than Westminster Hospital, and the problem is one of relative priorities within the available financial resources.—Lord CLITHEROE: May I ask the noble Earl whether he is aware that this hospital was only two-thirds built when the war broke out, that it is impossible for a teaching

hospital to do its work effectively unless it is a complete whole, and that in that respect the needs of this hospital have a claim above a great many others? Will he represent to the Minister that it is almost impossible for Westminster Hospital to plan its work and its future unless it is given some indication of when this problem will be resolved? If only some indication can be given, then a great deal of confusion will be resolved.—The Earl of ONSLOW: I am aware of the building situation. The Minister is taking a very lively interest in this matter. In fact, I understand that one of his medical advisers is visiting the hospital.

Malnutrition in Uganda

Mr. J. T. STONEHOUSE asked the Secretary of State for the Colonies, in view of the failure of the Uganda Government to deal with the problem of malnutrition, what action he now proposed to take to ensure that this problem is dealt with effectively.—Mr. A. T. LENNOX-BOYD replied: The Uganda Government recognise that the problem of malnutrition is a major one and that much remains to be done to combat it. But considerable measures have been taken by that Government, and I cannot accept the suggestion that they have failed to deal with the problem effectively. These measures include the establishment of a nutrition unit, the appointment of a scientific committee on human nutrition, the establishment of child-welfare clinics at all district hospitals, health centres, and dispensaries, the widespread distribution of milk powder (which will increase to over 600 tons by 1960), and increased education in health and nutrition.

Microbiological Research

Mr. EMRYS HUGHES asked the Prime Minister if he would consider transferring the duties of the Minister of Supply, in respect of microbiological research, to the Minister of Health.—Mr. HAROLD MACMILLAN replied: No, Sir. This research is undertaken for defence purposes. It therefore seems appropriate that it should continue with the Ministry of Supply. Any discoveries which have a bearing on general medicine are, however, made available to the medical profession, usually by publication in a suitable technical journal. Mr. HUGHES: Is the Prime Minister aware that there is widespread disquiet following the statement by an eminent and responsible Civil Servant and scientist that this department at Porton is manufacturing germs for plague, cholera, polio, and other dread diseases? If it is purely to defend the people's health, should not it be taken over by the Ministry of Health?—Mr. MACMILLAN: No, Sir. The only work done at Porton is to produce these bacteria in such quantities as to assess the threat which their use in war might represent and to aid research in providing defence against them. The material which may result from this work is made available through the various technical journals, and I think this system works satisfactorily.

Doctors in the Colonies

Dr. EDITH SUMMERSKILL asked the Secretary of State for the Colonies the number of physicians per head of the population in Kenya, Tanganyika, and Uganda, respectively.—Mr. JULIAN AMERY replied: In 1957, for every 100,000 persons in Kenya, Uganda, and Tanganyika there were respectively 8·7, 5·8, and 5·2 medical practitioners, including those practising under licence.

Dr. SUMMERSKILL asked what steps had been taken by the Department to encourage qualified doctors in the United Kingdom to take up temporary or other posts in Kenya, Tanganyika, and Uganda, respectively, during the years 1956 to 1958.—Mr. AMERY replied: The steps taken include advertisements and articles in the medical Press and arrangements for doctors to take up overseas appointments as an alternative to National Service. The response has been good. No difficulty is experienced in recruiting doctors for these Territories.

Ethical Pharmaceuticals

It is estimated that more than half, by value, of ethical proprietary preparations prescribed under the National Health Service are supplied by British-based subsidiaries of United States firms.

Closure of Tuberculosis Hospitals

In the last three years 55 tuberculosis and chest hospitals in England and Wales have been closed or had their use substantially changed.

Medicine and the Law

A Difference of Informed Opinion

A CHOLECYSTECTOMY was performed at Lewisham Hospital in January, 1956, on a 68-year-old woman under spinal anæsthesia supplemented by a light general anæsthetic. The following morning her left leg was found to be paralysed and, for a time, there was acute urinary trouble. She brought an action against the hospital management committee alleging negligence in the choice of the form of anæsthetic.

Mr. Justice BARRY, giving judgment for the defendants, said that it was beyond dispute that the injuries were caused by the dose of heavy 'Nupercaine' which was injected into the subarachnoid space in the plaintiff's spinal column.

An unusual feature of the case was that no criticism was made as to the manner in which the anæsthetic was administered, but it was contended that because of the known danger of permanent neurological damage a spinal anæsthetic should never be used for a high-abdominal operation, or at least should not have been used for an apparently uncomplicated cholecystectomy to be performed on a woman of the plaintiff's age and physical condition. A consultant anæsthetist was responsible for the choice of a spinal injection though it was administered by a senior house-officer. No-one suggested that the consultant was anything other than a highly competent anæsthetist or that he failed to acquaint himself with up-to-date techniques.

The courts could do no greater disservice to the community, or to the advancement of medical science, than to place the hallmark of legality on one form of treatment as opposed to another when there was a difference of informed medical opinion as to their relative merits. It would be intolerable for the courts to pronounce that a doctor was negligent because he adopted one alternative on the ground that the evidence in that particular case appeared to establish a balance of probability unfavourable to his choice. However, if a plaintiff suffered damage as a result of negligent conduct by a professional man it was the duty of the courts to ensure that he received proper recompense.

Was the procedure adopted in this case one which might reasonably have been employed in the circumstances by a competent anæsthetist using the ordinary degree of skill and care? To apply this test it was necessary to inquire into the state of medical knowledge, practice, and opinion at the time when the operation was performed. Seldom could a court have had more informed and helpful guidance. His Lordship had to consider whether the evidence established, not that the alternative method based on the use of muscle-relaxant drugs was on balance preferable to spinals, but that any doctor who chose a spinal anæsthetic in preference to a relaxant for this operation on this patient had on that account alone been guilty of negligence. On the whole of the evidence it would not be difficult to find that it might have been better for this operation to have been performed under a relaxant drug, but it was impossible to hold that the consultant's decision was a negligent one. If he had found for the plaintiff, he would have awarded £3000 damages.

Moore *v.* Lewisham Group Hospital Management Committee.—*Queen's Bench Division* (Barry, J.) Feb. 4, 1959. Counsel and solicitors: Maurice Lyell, Q.C., and Alan Lipfriend (Kingsbury & Turner); Montague Berryman, Q.C., and Michael Lee (Levett, Son & Hessenberg, Bromley).

EIRA CARYL-THOMAS
Barrister-at-Law.

In England Now

A Running Commentary by Peripatetic Correspondents

THE axe has at last fallen at the Medical Art Society; for the first time a hanging committee has been at work selecting. The advantages are obvious; but there is disadvantage, for any exhibition seen as a whole is apt to reflect the tastes of its selectors rather than the variety and interests of its participants, and in such an exhibition as this there is a natural inclination to choose the technically competent but stereotyped to the exclusion of the less talented but sometimes more vital. This exhibition has the stamp of the competent journeyman, particularly in the watercolour section, leaving more than a suspicion that some interest lies hidden in the *salon des rejets*.

Inevitably there is a tendency to seek, and little difficulty in finding, derivations. Once more we are reminded of the Douanier Rousseau and those who followed him by A. B. Hewlett in *On the Célé*, of Grandma Moses by S. L. Simpson's *Kitzbühel*. A strong trend to impressionism is natural in any " amateur " group; its most polished exponents are E. W. Peet with *Brixham* and *Street in Bombay*, and H. Neame with, appropriately, *An Impression*; A. M. Rackow might be considered expressionist in *Winter Morning*, *Wimbledon Common*. Realism is presented attractively through the agency of television masts in *Charm of Chelsea* by W. P. Kennedy, while J. J. Spira appears as a near tachist with his brightly coloured *Stage Set*; *Obsession* by J. Rostowski has an aptly selfconscious air about it; Margaret Little dons the abstractionist veil in *Painting—December '58*. Amongst numerous competent watercolours (*The Quarry* and *Provence Landscape* by L. Hoffman; *Suffolk Landscape* and *Connemara* by A. E. O'Donnell; *Norwich* by R. Rushton) *The Rock of Portugal* by Sir Philip Manson-Bahr gives pleasure, while *Southend-on-Sea, September*, evokes admiration for G. H. Rose's brave attempt at economy in line and wash. In the sculpture section G. Konstam succeeds with his vision of the *objet trouvé* in *Figure Dancing*, while A. Phillips' *Godiva Rests* maintains all the proprieties.

But it is to those pictures with the stamp of individuality that memory turns with the greatest clarity. The work of Ph. Tuttnauer has long had the mark of the professional whose intellect is brought to bear; this has been obvious in both the composition and the manner of his pictures. It is therefore of particular interest that this year he has abandoned *pointillisme*—very understandably since it had become an end-point. The result has been to emphasise the strength of his composition as in *Doctor's Workshop* (*1*) yet display a certain weakness of line; the very strength of his composition draws attention to the disappointment in *Doctor's Workshop* (*2*)—the empty uninteresting Winchester bottle placed at the focal point. Head, heart, and hand are conjoined in B. N. Brooke's enigmatic *Valley of the Shadow*. Here perpetual creation is implicit in the lily rising from the debris of a T. F. Powys graveyard; the symbolism is overt, the detail subtle, and the construction ingenious. It is excellently painted but ineptly framed. T. B. Anderson's *Stonemason's Cottage* in watercolour is painted with such fluidity as to impart real lyricism, while close by is another ink and wash of quieter charm—*Wilkin Valley* by Sir Harold Gillies. R. Fidler's drawing *Isolation* should be an encouragement to diffident beginners (and to selectors!), for despite uncertain draughtsmanship the strength of its impact and the emotion it evokes denote a moment of artistic vision. *Epping Forest* by G. H. Rose derives immediate appeal from individuality of execution, which is not, however, sustained owing to lack of a focal point. Quite the best portrait comes from the palette of Charles Wells, whose *My Line* is painted with as much assurance as his *Professor Norman Capon*.

* * *

It is always fascinating to listen to people talking in an unknown foreign language. Though one does not understand the sense, one can yet catch a glimpse of meaning of some phrases, and even perhaps some of the beauty of the poetry. But I wonder how many people recognise the following:

" Oue Tahde na ah in edde, anno de Di na, I tidde tah, I du de di on eet a te e edde, te ut te da oue dade ded, e didde oue tetedde a ne ahdin to te tetedde adase ut, ne no te tetate, ninne utte enu, to I ah te nini, poue e dordy, to edde e edde, Ame."

It comes from Allbutt and Rolleston's *System of Medicine*, and was written by Dr. W. S. Colman, who in 1911 was physician to St. Thomas's and to Great Ormond Street. As he says, strange as this looks and sounds, it will be found that there is method in it. The patient is unable to pronounce many of the consonants and substitutes for them t, d, or n. It is of particular interest to me, for I had speech difficulty rather of this natufe, and for many years, without being blasphemous, thought that God's name was Harold. Perhaps this shows that I was able to say the Lord's Prayer a little more intelligibly than Dr. Colman's patient who had idioglossia.

* * *

The report of a case of a cycle susceptible to coloured nylons (Feb. 7, p. 307) has altered the lines of investigation into cycle speed at a large number of centres.

We (me et al.) spent last weekend letting off 50 nurses in brightly coloured nylons along the High Street at alternate hours (so as to give a control hour when no nylons were visible). Our results show that all male-type cycles increase their speed by significant amounts during the period that nylons are displayed. Workers abroad, we learn, using batches of 50,000 nurses in a range of a hundred different coloured nylons are getting similar results, with interesting minor variations depending on colour and shape.

The mention of an old gentleman proceeding, apparently spontaneously, at great speed has recurred both in our series and in that from abroad. An ophthalmological colleague suggests that this apparent anomaly is due to a high incidence of presbyopia among aged cycles. This condition makes them prone to hurry towards distant objectives, while younger machines are engrossed in the study of their immediate environment.

In the light of these further studies, the first law of cycle behaviour may now be formulated as follows:

The speed of male cycles is directly proportioneal to the size, shape, colour, and speed of travel of the nylons one female cycle ahead. A minor exception to the law has been found to occur should the male-type cycle have a female-type rider, but no doubt the reason for this will soon occur to someone. The speed of female cycles is so far totally unpredictable.

* * *

My daughter—a final-year medical student—acted as a locum house-surgeon for eight days just before Christmas. She was doing a midwifery job and was actually working or on call, sleeping beside the maternity ward, for 134 hours. She has now received the following statement from the hospital:

	£	s.	d.
Gross pay	1	2	10
National Insurance		16	0
Superannuation		3	3
Net pay		3	7

A cheque for 3*s*. 7*d*. was enclosed, her reward (apart from the modest board and lodging provided) for her work. Admittedly she was unlucky; as her span of duty included two Mondays, she had to pay two N.I. contributions. Full marks for efficiency, however, go to the Inland Revenue Department, who have already written to inquire about her earnings as a locum; perhaps tax should have been deducted at the source.

* * *

In the Garden—II.

OBSERVATION

Chaps who call it *Iris stylosa* tend to be tough
And plant it in rubble and trample on it and generally treat it rough;
But chaps who pronounce *stylosa* as *unguicularis*
Say that manure and watering and constant daily care is
The secret of success. But I've tried both these cults,
With no results.

Letters to the Editor

STAPHYLOCOCCI IN HOSPITALS

SIR,—There is one potent source of cross-infection by drug-resistant staphylococci for which there is at present no practical means of control—namely, the patient with chronic staphylococcal infection such as osteomyelitis.

Many of these patients are children who must spend long periods in hospital, commonly in general wards, and they are often incurable.

Since it is cruel to isolate them singly there is surely a case for creating special centres, as was the practice previously with tuberculosis. It seems to us that the setting up of centres for such cases follows logically from the Cohen report,[1] and should be given immediate attention, We are, in fact, suggesting that there should be staphylococcal sanitoria, and we would welcome comments from those interested in this problem.

Royal South Hants Hospital, Southampton. EDWARD S. DUTHIE.
Royal National Orthopædic Hospital, Stanmore. CHARLES H. LACK.

SIR,—My own observations have been amply confirmed from many sources, and there seems no doubt that many hospitals are far less clean than they should be. This is not just a matter of æsthetic importance but constitutes a very real danger to patients. In hospitals there tends to be an especially heavy concentration of dangerous bacteria, and there is no doubt that dust and dirt facilitate cross-infection. Those who, like myself, have had to treat the fulminating cases of staphylococcal enteritis striking down those in their prime of life, sometimes after a straightforward operation, have some idea of the potential gravity of the situation. Up and down the country many tragedies have been enacted as a result of cross-infection, particularly by virulent staphylococci.

There is a natural tendency not to publicise such cases, as one has a responsibility to maintain the confidence of the population in the hospital.

The root cause of dirty walls has been the lack of interval cleaning of wards and departments by porters and cleaners, and little if anything is done between one "spring cleaning" and the next. In the course of 12–24 months a great deal of dust and grime can accumulate, particularly in smoky districts. It is clear that hospital secretaries have been reluctant to use porters and cleaners in view of the ambiguous and misleading Ministry directive H.M.C./52–123, and it is evident that the Painters Union has taken full advantage of this ambiguity to press their monopoly. The uncooperative attitude of the painters must have been only too obvious to those who saw their secretary on television.

As a result of recent publicity, hospital secretaries may now feel on safer ground if they use porters and cleaners as much as possible for the cleaning of walls and paintwork in the interim period between major "spring cleaning", which naturally has to be done by painters. I was particularly interested to hear of one hospital which has organised a weekly mopping of all walls to the ceiling with long-handled specially impregnated mops, and some hospitals are beginning to use vacuum brushes. There appears to be a lot of readily available information about the newer techniques for the control of dust and dirt.

The publication of the Cohen report will provide the opportunity for all medical committees to review the general hygiene arrangements in their hospitals. The prevention of cross-infection is a complex matter needing much attention to detail, such as the method of cleaning of blankets, the technique of ventilation of theatres, and the treatment of floors, as well as the general eradication of dust and dirt. In addition, there are many little practical points which physicians and surgeons can usefully discuss. I hope that in future the senior medical staff in hospitals will accept a direct responsibility for ensuring a proper standard of cleanliness in their wards or departments, and will encourage the appointment of a hygiene officer who can make a report every three or six months to the committee.

Central Middlesex Hospital, London, N.W.10. F. AVERY JONES.

SIR,—In reply to Dr. Avery Jones (Jan. 24) of the Central Middlesex Hospital, I am surprised that a member of an organisation which operates a very "closed shop" should have the impertinence to interfere with another organisation's business who are dealing with the livelihood of their members.

The Medical Profession are fully aware that there are now agreements on the conditions of employment for all types of people employed in hospitals and it was obvious, when I met Dr. Avery Jones at the television studios, Alexandra Palace, that he had been misinformed with regard to the question of shortage of labour; in fact, last winter, there were 4000 painters registered as unemployed and, indeed, at the present moment, painters head the list of tradesmen unemployed in nearly all labour exchanges.

I fully agree with the doctor for the need for keeping the walls clean in the hospitals and, in fact, as a visitor to many hospitals, I am informed by most managements that they are in arrears with their maintenance work due to the limitations imposed by the Chancellor in the grants allocated through the regional boards.

Under these circumstances, I would suggest to the medical profession that they should assist in bringing pressure on the Treasury to obtain more money for maintenance work in the hospitals and not attack the livelihood of craftsmen who already suffer from casualisation in their industry.

I am sure that my organisation would welcome a more regular cleaning of hospital walls and are always prepared to deal sensibly and reasonably with any hospital who has a problem but, what we have found up to date where there has been complaints is—that the hospital management committee have blatantly attempted to abuse the agreement and, in fact, one committee said that "they were going to do as they liked," and I think you will agree, in such circumstances we, like the medical profession, are insistent that agreements entered into should be carried out in a proper manner.

I trust that your readers will note that it is illogical to talk of "restrictive practices" when it means, in fact, a member of the medical profession is attempting to encourage people to disregard arranged agreements.

National Society of Painters, London District Committee, 48, Grafton Way, London, W.1. E. G. YOUNG Organiser.

SIR,—I am most surprised that the letters of Mr. Stanley Way (Jan. 10) and Dr. Avery Jones (Jan. 24) have provoked so little support, for there must be few doctors working in hospitals who have not encountered this problem of dirty wards. In the "bad old days" a clean ward was a ward sister's pride, and most of the cleaning was done by the nurses. Quite rightly, cleaners were later employed to take over these menial duties, but there must be few who would claim that the change has been for the better, particularly in recent years.

I cannot help thinking that the advent of antibiotics has closed the eyes, particularly of the more recently qualified, to

1. Central Health Services Council: Standing Medical Advisory Committee. Staphylococcal Infections in Hospitals: report of the Sub-committee. H.M. Stationery Office, 1959. See *Lancet*, Jan. 24, 1959, p. 185.

the necessity for hospital hygiene. The emergence of drug-resistant organisms, particularly the staphylococcus, is once more seriously worrying all those whose task it is to combat infection.

I, too, have experienced the difficulties mentioned by the above correspondents. My maternity department has a mammiliform tide-mark around its walls: below, reasonable cleanliness; above, dirt. At first I was told that the cleaners were not insured against falls from step-ladders. I therefore suggested the use of long-handled sponge-mops, only to discover that the washing of the upper part of the walls was the prerogative of the painters. The illogicality of this restrictive practice is apparent: if the upper part of the walls must be cleaned by painters, why not the whole wall? Conversely, why can the cleaners not do the whole wall?

Where does this nonsense end? Will the electricians claim that only they must clean the electric-light shades, or the plumbers the sluices and closets? Why should not the terrazzo floors be washed by the masons, the wooden floors polished by the carpenters? The possibilities are almost endless.

The solution of this problem is not by the provision of long-handled mops, but by a return to sanity. Let the cleaners union (if any there be) insist that their members be allowed to clean, and let the painters stick to their job—the preparation for painting, and the actual decoration of the hospitals. Is our great administrative army helpless against the demands of the unions?

One final point: the problem is vastly accentuated by the size of the wards in our ancient hospitals. May I make a plea that in future hospital planning small ward units be built which can readily be closed for cleaning without the temporary loss of too many beds.

Rochester, Kent. STANLEY W. WRIGHT.

SIR,—Your account (Jan. 31) of the recent Birmingham conference, though ably written, may by condensation give rise to misconception.

First, as regards the experiments by Dr. Lowbury and Dr. Sevitt, in which contamination was found in about 20% of surgical wounds immediately after incision and in nearly 60% before sutures were inserted: these contaminants, it must be emphasised, were almost always saprophytes, and usually scanty; staphylococci were rare. On the subject of skin disinfection, the demonstrated effectiveness of 1–2% iodine in 70% alcohol is somewhat offset by the occurrence of skin reactions to iodine: the value of such alternatives as 0·5% chlorhexidine in alcohol and the iodophores requires careful study. For the surgeon's hands, hexachlorophane soap has been found to reduce the bacterial flora only if it is used consistently; its value is still a subject of controversy.

Some have read into your report of my remarks a suggestion that I consider the pathologist should be the responsible executive officer. I feel most strongly that executive responsibility should rest with administration (be it medical, nursing, or lay) but that the pathologist should be responsible for advising and warning and also should be consulted (a royal role, I believe).

At the request of the S.A.M.O. I am editing the proceedings of this meeting for publication as soon as possible, and those who wish will have the opportunity of studying the full report with discussions.

Pathology Department,
Selly Oak Hospital,
Birmingham, 29. KEITH THOMPSON.

FIFTY YEARS OF THE SCHOOL HEALTH SERVICE

SIR,—The golden anniversary of the School Medical Service, as noted in your leading article on Jan. 31, is an appropriate time for congratulations on the achievements of the past and for reflections on the future.

The service has undoubtedly achieved much in the past, bearing in mind its original aims to detect defects and improve the physical, mental, and moral conditions of children; and in recognising all the improvements we have also to remember the social and medical situations of that period. Fifty years ago poverty was widespread, and many families could not afford the luxuries of taking the children to the doctor. Fifty years ago the causes and the pathology of many of the common childhood diseases were unknown, and treatment was largely empirical and symptomatic. Now, some fifty years later, there is a National Health Service with full medical care available to all the population, our knowledge of pathology is advanced, and we have many specific drugs available to treat the majority of the common infections. What is the place of the School Medical Service in the present medical set-up? How does it fit in with developments in relations between patients and their family doctors?

Since 1948, when the National Health Service was started, family doctors have had opportunities of developing and improving their relations with their patients, and many have seized these opportunities to perform increasing numbers of services for their patients. Many family doctors organise their own maternity and infant-welfare clinics and could easily do the same for the schoolchildren in their practices. Opposed to all this has been the tendency of the N.H.S. towards tripartite administration of general practice, hospitals, and public health; and as a result, with regard to the School Medical Service, there is often little personal contact between the family doctors and the school doctors. Some actions of the latter run counter to the wishes of the family doctor, with consequent irritations of the doctor and confusion of the parents.

What are the present aims of the School Health Service and how far are they being achieved? It seems to me that this service is largely based on series of medical inspections to pick out early defects, but in spite of some fifty years of activity there has been very little satisfactory critical analytical work carried out as to how successful all this has been in relation to the time, energy, and money that have been spent. To a lesser extent the service is endeavouring to teach health to schoolchildren and to assist in resolving the problems of the individual in school.

These admirable aims must still be pursued; but is there still need for all the work to be carried out by special school medical officers? Could not the bulk of the work be undertaken by the family doctors? Under the N.H.S. each and every school child has his or her family doctor who is well known and who knows the family background and problems. With a view to developing and improving doctor-patient relations why should not the family doctor be allowed and encouraged to carry out the periodic routine medical examinations on all the schoolchildren in his practice. For these examinations he should be entitled to an agreed fee, which would at the same time help develop relations with his patients and also act as an incentive to a wider range of service by him. The sceptics will at once say that the family doctors are far too busy, quite untrained, and quite unsuitable, and in any case would not wish to carry out such a service. To this I would only answer that talking to many of my colleagues they all seem convinced that, given the opportunities, they could carry out such examinations quite easily. For such work to be successful much would depend on the energies and initiatives of the local medical officers of health in establishing and maintaining good liaison with family doctors. It seems useless to argue over the theoretical possibilities of any such system; the only way would be to try it in an experimental area.

Even if family doctors would undertake the routine examinations of all schoolchildren in their practices there would still be a need for the School Medical Service, but with a much smaller staff. It would be needed to supervise and assist the family doctors in their work and allow easy access to special diagnostic and therapeutic clinics. It would be needed to develop its great opportunities in carrying out health education

in the schools in close cooperation with the teaching staff. It would have an important role in acting in consultation with the schoolteachers and the family doctors and parents to settle the various problems of individual children at school.

Sir John Charles writes in the report that was the subject of your leader: "It would be strange after 50 years if there were no need to alter techniques". I would like to see this challenge taken up by individual local authorities and a series of experiments undertaken on the best methods of using the available health services for the welfare of the schoolchild.

Beckenham, Kent. JOHN FRY.

MENTAL HEALTH BILL

SIR,—I would like to draw attention to clause 4 (1) which reads as follows:

"In this Act 'mental disorder' means mental illness, arrested or incomplete development of mind, psychopathic disorder, and any other disorder or disability of mind; and 'mentally disordered' shall be construed accordingly."

It would appear that this term is intended to be comprehensive and to include all levels of mental subnormality.

With the formation of a Parents' Association at this hospital some 12 months ago, I have had an opportunity as their president of appreciating the parents' views on classification and terminology.

There is no doubt that the classification and terms used in the Mental Deficiency Acts, 1913–38, caused much hurt and resentment to parents and relatives. On the other hand the term "mentally handicapped", while reasonably descriptive, is quite acceptable and is indeed regularly used in the publication *The Parents Voice*.

As the Bill is now in the committee stage I would strongly urge that further consideration should be given to the question of terminology, and that in the Act itself the term "mentally handicapped" should be used to cover all cases of intellectual retardation admitted to our type of hospital.

Bromham Hospital, near Bedford. T. A. DANBY.

SUPPLY AND DIETARY USE OF FATS

SIR,—Since Dr. Sinclair's previous letters show that he does not pull his punches, there is no reason why others should do so; and it does not take an Ancel Keys [1] to give excellent reasons for refusing to accept Dr. Sinclair's instructions (Jan. 31) on which fats we in this country should eat and not eat in order to avoid coronary-artery disease. Such instructions appear to offend the laws of Nature and even the canons of common sense.

We are told, for example, that "many fish are excellent sources of essential fatty acids but the fat of beef and mutton is not, although by research this defect may become manageable". What a colossal piece of impertinence this appears to be! For, to transcribe this assertion into simple language, where the meaning cannot be shrouded in a mass of chemical formulæ, we are told that Nature is wrong and that Dr. Sinclair (who, it will be remembered, makes no distinction between the protective fat occurring so wonderfully in certain wild animals and the obesity occurring in civilised man [2]) is right; that the natural instinct of appetite, exerted on such wholly natural materials to us in these islands as beef and mutton fat, should not be followed, and that we should eat, instead, sunflower-seed oil and other materials wholly alien to us. The sunflower, for example, comes from the New World; what truck have we, evolved in the Old World and adapted to the fats thereof, with this stuff? If these extraordinary and most unnatural substitutions proceed further, the volunteers in nutritional research may become scarcer, and the emigration of workers in this field even faster, than Dr. Sinclair describes.

As I asked in an earlier letter,[3] in connection with researches that ignore the basic considerations of evolution, how can the tactics be correct when the overall strategy can be proved incorrect; how can the tree be right when the wood can be proved to be wrong?

Nor is there the slightest need for these deep conflicts to arise. If an excess consumption of fat is concerned in the production of coronary-artery disease, to which certain facts do appear to point, it is perfectly feasible to correct this by natural methods, as I have tried to show [4]—and which almost anyone else interested in the evolutionary approach could have shown very much better. The medical methods change every year; the natural ones never do. There is ample scope for reducing fat consumption in these islands this way, without ever breaking evolutionary laws or sacrificing some of the pleasures that still remain to us. And exactly the same approach is possible if the quality, rather than the quantity, of the fats is in question.

H.M.S. *Dolphin*, Gosport, Hants. T. L. CLEAVE.

1. Keys, A. *Lancet*, 1956, i, 576.
2. Sinclair, H. M. *ibid*, 1958, ii, 1065.
3. Cleave, T. L. *ibid*. p. 420.
4. Cleave. T. L. Fat Consumption and Coronary Disease. Bristol, 1957.

ASPIRIN AND ITS DOSAGE

SIR,—Aspirin (acetylsalicylic acid) is perhaps the most used drug in modern life. The interesting thing is that in spite of its protean use its pharmacology is either unknown or baffling in its simplicity. To some patients it is a miracle worker, to others it is a drug which is used in great quantities without much effect. From my experience the secret is in the dosage; in fact, in my opinion the most potent analgesic dose is a small one in the region of gr. 5 (one tablet).

When joining an old-established practice nearly thirty years ago, I found in the dispensary two well-used tablets: Dover and aspirin and aspirin aromaticus (aspirin gr. 5 with an aromatic base). To my surprise they were effective in doses of one tablet even with patients who said that aspirin did no good. This appeared to be suggestion, until the time came when I suffered myself from toothache off and on for a year or two. As it was a chronic condition I was careful and tried one aspirin, with absolute success. If for any reason I tried two I found them ineffective. Now I have for years ordered aspirin to be taken in gr. 5 doses to be repeated after an hour—usually, needless to say, in a disguised form. Lately I have been able to openly prescribe one tablet to patients and to confirm that this is the best dose.

What is the rationale behind this? There are two possible explanations. Firstly, that, as with potassium iodide, doubling the dose decreases its effect, perhaps by encouraging its elimination. The second explanation is probably the correct one. Asprin has two actions, both analgesic and antipyretic. If the pain is inflammatory, then the antipyretic action, by increasing the blood-supply to the inflamed parts, will increase the pain (it can be considered that the antipyretic action is due to superficial dilation of the blood-vessels).

Aspirin has lately been coming back to favour; it is used extensively in chronic "rheumatism", and is held to have a "cortisone-like" effect—surely an odd inversion. Personally, I find that aspirin gr. 5 three times daily is very effective in the treatment of chronic rheumatism and osteoarthritis. Most patients benefit from a reduction from gr. 10 to gr. 5.

For the last thirty years, new makes or forms of aspirin have come on the market, swept all before them, increased their sales to an astronomical degree, and then subsided to large regular sales. In all these the dose was given as in the region of gr. 5 in the original advertisement.

Petworth, Sussex. W. ANTONY BALL.

DEXAMETHASONE

SIR,—The interesting article by Dr. Slater and his colleagues (Jan. 24) will draw attention to the availability of yet another new corticosteroid for the treatment of asthma, rheumatoid arthritis, and many other disorders. Since this substance became generally available, a few weeks ago, I have seen several patients whose condition has deteriorated since being transferred to this new drug, owing to the fact that it was not sufficiently appreciated by their physicians that one tablet of this substance (0·5 mg.) is not the therapeutic equivalent of one tablet of cortisone (usually 25 mg.), hydrocortisone (usually 20 mg.), prednisolone or prednisone (5 mg.), or triamcinolone or methyl prednisolone (4 mg.), but is only just over half as effective.

This, the most potent of the available corticosteroids, because of this difference in tablet strength and despite adequate instructions regarding dosage sent out by the makers, tends to be given in too small dosage; relapse is occurring not infrequently because of inadequate dosage, the change from the previous corticosteroid being made often on a tablet-for-tablet basis. Two tablets of dexamethasone is, perhaps, slightly more effective than one of the others mentioned, but only just so; the dose ratio is perhaps 5 mg. prednisolone or prednisone to 0·8–0·9 mg. dexamethasone. In practice this means roughly doubling the number of tablets given on changing from any of the other available corticosteroids. The patient may well wonder, if this is the strongest substance of its kind available for treatment of his disease, why he has to swallow twice as many tablets of it.

London, W.1. F. DUDLEY HART.

EXPERIMENTAL SHOCK

SIR,—I was interested in your leading article on this subject.[1]

You review the observations of Ochsner and his colleagues in several series of goats subjected to massive injury of the thigh of a degree sufficient to lead to the death of all of the animals.

You make much of the prolongation or decrease of survival-time compared with a group of control animals. But the only animals that survived the shock period were those subjected to bilateral amputation of the hip-joints together with other forms of treatment.

It seems important to remember that these animals had been subjected to an injury uniformly fatal, except with such heroic treatment. The average survival-time of the control group was 19·6 hours. Treatment that was found to extend survival-time significantly prolonged this time on average from 4 hours to 3 days and $3^1/_2$ hours. Is it valid to conclude that measures which altered the survival-time of animals thus injured would similarly affect the mortality-rate of people or animals subjected to trauma resulting in less than 100% lethality? Is the observation that dextran alone reduced the survival-time from 19·6 hours to 16·1 hours in fatally injured animals applicable to patients with a real chance of recovery if properly treated? Granted that this work was a serious and potentially valuable attempt to gain information on a subject most difficult to investigate, are increases of survival-time in fatally injured animals more than indicators of a direction for further investigation?

Local wound cooling increased survival-time and permitted postponement of debridement for as long as 24 hours. There is an interesting parallel to this in work on experimental rabies in which systemic cooling of the laboratory animal also significantly increased survival-time. But no-one would infer from this that systemic cooling is an effective method of treating rabies.

1. *Lancet*, 1958, ii, 784.

It has long been recognised in experimental biology that series based upon an L.D.$_{100}$ can lead the investigator far astray. Had these series been based upon injuries that would lead to approximately an L.D.$_{50}$, and had the conclusions been drawn from significant increases in the percentages of animals surviving, would not the findings have been of considerably greater significance to the patient sustaining something less than a fatal injury?

Office of Medical Defense,
New York State Department of Health,
Albany, N.Y. JAMES H. LADE
Director.

A "CHEST SERVICE"

SIR,—Your leader last week on this subject appears to complicate the situation unnecessarily. Almost 30 years ago I advocated that the old name tuberculosis dispensary should be dropped and replaced by the modern designation chest clinic. In fact, the public-health department of the county borough of East Ham, through the cooperation of the then medical officer of health, permitted me to make this change as far back as 1930. I had then already been made fully aware, through representations of the family doctors and their patients, of the opprobrium attached to "tuberculosis dispensary" and of the consequent difficulty in referring patients there. Even though at least 75% of such patients were either free from disease or were suffering from something other than pulmonary tuberculosis they regarded themselves as potential social lepers.

I was, therefore, somewhat amused to receive 20 years later a circular from the regional board notifying me that "tuberculosis dispensary" was to be dropped in favour of "chest clinic".

I well recall reading a paper[1] to the then Tuberculosis Association (now the British Tuberculosis Association) on Problems of Differential Diagnosis at a Tuberculosis Dispensary. I then discussed the risks inherent in specialisation and described how pulmonary tuberculosis may simulate any other disease of the respiratory tract or, indeed, of general medicine. I quoted cases I had encountered of disease in the upper air passages, many bronchopulmonary diseases, certain diseases of the cardiovascular system, congenital and acquired, thyrotoxicosis, and a number of general constitutional diseases. The late Sir St. Clair Thomson, in the chair, and Sir Robert Young who was present at the meeting were among other experts sympathetic to the idea of a change of name. As Osler wrote, "the incessant concentration of thought upon one subject, however interesting, tethers a man's mind in a narrow field". Some degree of specialisation there must be, but I hold very strongly that the medicine of the future should be an integrated social and clinical medicine in which the family doctor has a recognised role.

It has been said that a major defect in the National Health Service is excessive concentration on individual illness at hospital level instead of coordination between the hospital, local-authority, and general-practitioner services, thereby enabling prevention, diagnosis and treatment, and aftercare to be considered as one continuous process. Only by this means can the problem of relapse in relation to many diseases of chronicity—thoracic, gastrointestinal, rheumatic, &c.—be combated.

If these criteria are accepted the concept of an adequate chest service for the nation becomes clear.[2] You, Sir, recognise chest medicine as a legitimate branch, and the Joint Tuberculosis Council has made a timely recommendation that the integration with general medicine that has already begun should be continued. Further efforts should be made to bring chest clinics "within the curtilage of general hospitals" and tuberculosis should "no longer be dealt with by a body of physicians isolated from general medicine".

1. Ellman, P. *Tubercle, Lond.* 1929-30, **11**, 531.
2. Ellman, P. *Postgrad. med. J.* 1945, **21**, 331.

During the last decade we have witnessed stupendous changes in all branches of thoracic medicine, and, without being complacent about tuberculosis, we cannot ignore that 25,339 deaths twenty years ago have now diminished to 4784. In the same period lung cancer has increased its toll from 4658 to 19,119, while deaths from chronic bronchitis are in the region of 30,000. The contemporary chest physician must have a sound knowledge of general medicine and include within his purview the wide field of applied respiratory physiology, thoracic surgery, chest radiology, and, in fact, all organs within the thoracic cage.

We can achieve a comprehensive chest service, as I outlined in an address to the Royal Institute of Public Health,[3] and coordinate it with other branches of medicine both by utilising those existing well-staffed and well-equipped chest clinics, chest units, and hospitals, and chest departments existing in general hospitals, according to existing local facilities, but their final integration within the hospital service is inevitable.

London, W.1. PHILIP ELLMAN.

SERUM-TRANSAMINASE LEVELS

SIR,—The spectrophotometric method of Karmen [4] has been adopted, with modifications, as the standard procedure for determination of serum-glutamic-oxaloacetic-transaminase (S.G.O.T.) and serum-glutamic-pyruvic-transaminase (S.G.P.T.). The colorimetric method of Reitman and Frankel [5] has more recently been adopted as a routine procedure for these estimations, with the recognition that though more convenient it is less accurate. We consider that Reitman and Frankel's procedure of expressing their results in Karmen spectrophotometric units (1 unit equals a decrease in *optical density* of 0·001 per ml. of serum per minute under the conditions of the test) is valuable and should not be discontinued. Dr. Daly and Dr. Jordan (Jan. 31) propose that the units of King [6] be adopted for the colorimetric assays: these are based on measuring the quantity of reactant formed and not the rate of utilisation of reduced diphosphopyridine nucleotide and are therefore theoretically more valid. Nevertheless their introduction would cause great confusion and the need to learn two sets of normal ranges and of abnormal responses.

Our laboratory uses for S.G.O.T. or S.G.P.T. the Reitman and Frankel method in routine, and the Karmen method for checking unusual results and for research.[7] To have a different unit for each type of analysis would make comparison impossible within the laboratory, and between different laboratories using different methods. We have found excellent comparison between results with the two methods up to about 120 units. With sera of greater activity the colorimetric method is less accurate [8]—but this is a shortcoming of the method and not of the system of units.

Standardisation of temperature is more important. Temperature correction is essential because of the great difference in activity of transaminases at different temperatures. In the colorimetric method incubation takes place at 37°C, and a factor corrects the readings to spectrophotometric equivalents at 25°C. The standard temperature used seems to depend on the latitude, and efficiency of central heating or air-conditioning, of the laboratory; we presume that most workers would use a standard temperature which is about the average of their cuvette temperatures. We use 20°C[7]; others have used 23°C[9] and 25°C.[10] It would help comparison of results from different laboratories if there were an internationally agreed standard temperature. We would like to suggest 22·5°C (72·5°F), but would be interested to have the views of other workers.

Department of Chemical Pathology, Royal Free Hospital, London, W.C.1. D. N. BARON JOYCE BELL.

TESTOSTERONE IN DEFECTIVE SPERMATOGENESIS

SIR,—Whilst those who work in infertility clinics will agree with Dr. Powell's suggestion (Jan. 24) that " fathers are not always husbands ", it does not necessarily follow that a man with apparent azoospermia on laboratory semen analyses cannot produce spermatozoa during normal coitus.

Dr. Spence and Dr. Medvei (Jan. 31) say that " his comment surely cannot apply to all nine patients with sperm-counts of 10,000,000 per ml. or less ". I have already published accounts of pregnancies achieved with sperm densities of presumably less than 1,000,000 per ml., and so have many other workers. I can record one case of apparent azoospermia in which something like nine semen analyses performed at four different hospitals had always revealed total absence of spermatozoa, and yet the post-coital test showed their presence. The domestic circumstances of this man and his wife were such that there was no doubt that he was the father of this particular child when his wife conceived after treatment for cervicitis.

There must be many like myself who, if they have worked for many years on infertility, must be confronted from time to time with a man who has difficulty in ejaculation although the rest of the coital act appears normal. These difficulties appear to be increased when providing a specimen for laboratory analysis, and I therefore do not consider it quite so much beyond the bounds of possibility that this azoospermic patient of Dr. Spence and Dr. Medvei was indeed the father of that particular child. It would be interesting to know whether Spence and Medvei did a post-coital examination of the urine of this man, in case his proved to be one of those rare cases of retrograde ejaculation of the semen into the bladder, and also to know if spermatozoa were found in his wife's post-coital test.

Manchester. BERNARD SANDLER.

MITRAL VALVOTOMY IN THE YOUNG

SIR,—Dr. Gray [11] states that " 40–50% of adults undergoing mitral valvotomy have histological evidence of active rheumatic carditis ". I assume he refers to studies of biopsy specimens of the left auricular appendage obtained during this operation.

If this assumption is correct, the figures quoted are far in excess of what has been found at autopsy. Patients with mitral valvular disease who come to autopsy with no clinical evidence of active rheumatic fever commonly show no morphological evidence of " active rheumatic carditis ".

A number of possibilities exist to account for the figures cited: (1) the auricular appendage is unique and responds differently to the ventricles; (2) autopsy material is not representative of the rheumatic process; and (3) histological criteria are more easily fulfilled in the appendage. Careful histological analysis of 680 auricular appendage biopsies [12 13] secured during surgery has negated the above possibilities. Utilising strict morphological criteria, and directing attention to (1) the life cycle of the Aschoff body, (2) topography of the left auricular appendage, and (3) histochemical data, only 2% were considered as diagnostic of active rheumatic carditis. The mere presence of an isolated Aschoff body in the absence of associated inflammatory and degenerative changes cannot be regarded as

3. Ellman, P. *J. R. Inst. publ. Hlth*, 1954, **17**, 217.
4. Karmen, A. *J. clin. Invest.* 1955, **34**, 131.
5. Reitman, S., Frankel, S. *Amer. J. clin. Path.* 1957, **28**, 56.
6. King, J. *J. med. Lab. Technol.* 1958, **15**, 17.
7. Baron, D. N., Alexander, C. P., Bell, J. L., Oakley, C. M. *Quart. J. Med.* 1958, **27**, 533.
8. Mohun, A. F., Cook, I. J. Y. *J. clin. Path.* 1957, **10**, 394.
9. Wroblewski, F., LaDue, J. S. *Proc. Soc. exp. Biol., N.Y.* 1956, **91**, 569.
10. Steinberg, D., Baldwin, D., Ostrow, B. H. *J. Lab. clin. Med.* 1956, **48**, 144.
11. Gray, I. R. *Lancet*, 1958, ii, 1263.
12. Tedeschi, C. G., Wagner, B. M., Pani, K. C. *A.M.A. Arch. Path.* 1955, **20**, 408.
13. Wagner, B. M. *Circulation*, 1958, **18**, 791.

" active " disease.[14] One is impressed with the terms " Aschoff-like " and " possible or probable Aschoff body " which occur in published reports on this subject.

The application of the classic histopathological requirements and the dynamics of the rheumatic process should result in a much lower figure than that reported by Dr. Gray.

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MANAGEMENT OF CIVILIAN LIVER INJURIES

SIR,—Reading Mr. Grahame's article of Dec. 20 reminded me of an interesting case seen during my internship two years ago.

A young Mexican-American male, about 30, was brought to our hospital after he was knocked down by an automobile. His only complaint was pain in the right upper quadrant, aggravated by deep inspiration. The rest of the medical history was negative. The patient was unemployed and lived in a cheap hotel on " skid row ".

He was a husky, well-nourished man, who was in moderate discomfort. He attempted to splint the right upper abdomen with his hands and by breathing shallowly. The entire right upper quadrant was tender, and crepitation was felt when the rib margin was palpated. Blood-pressure was normal; pulse-rate 100 and regular.

Because of a slight rise in the pulse-rate the abdomen was explored under general anæsthesia through a midline incision. A small amount of clotted blood was found. Fragments of a fractured rib had produced what appeared to be a superficial laceration of the surface of the liver, and though this was no longer bleeding a piece of gelatin foam was sutured over it. Apart from this injury, the liver seemed normal. While exploring the abdominal organs for other evidence of trauma a small piece of tissue measuring about $1 \times 1 \times {}^{1}/_{2}$ cm. was found. It was brownish and had the appearance and consistence of devitalised liver tissue. We were unable to locate the site of dislocation of this piece of tissue. The specimen was sent for pathological examination.

The patient recovered rapidly and wanted to go home the day after the operation. Because of a mild fever he was persuaded to stay. In a week the sutures were out and he was ready for discharge. He was discharged to a tuberculosis hospital. The dislodged liver tissue was found to be involved in " a miliary granulomatous infiltration compatible with miliary tuberculosis ".

Cook County Hospital,
Chicago, Illinois. HAROLD LEVINE.

CIRCULATION OF THE BLOOD

SIR,—It appears to be high time that the mechanism of the circulation of the blood was re-examined.

On purely physical principles it seems highly unlikely that the myocardium, sometimes remarkably thin and weak, is able to provide enough power to drive a large quantity of viscous fluid through a vast number of small holes. The muscle of the arterial wall must play a much larger part in circulation than the commonly suggested regulation of flow by constriction and dilatation. I should like to submit the following theory for comment and criticism.

When the pulse-wave causes a local dilatation of the artery, this is sufficient to touch off an active contraction of the smooth muscle of the arterial wall, so that each pulse-wave proceeding down the artery is followed immediately by a wave of positive contraction, thus producing a milking effect, with positive propulsion of the blood with each beat.

The tone and state of irritability of the arterial muscle is therefore a matter of great concern, for poor tone, as in the depressed, will lead to poor peripheral circulation, and there will therefore be some sense in the administration of strychnine-containing tonics for the debility following influenza and other infections.

Increased irritability of the arterial muscle, as in anger, would first produce an increase in the milking effect and thus a peripheral flush; with increasing and persistent anger the irritability may increase to the point where constriction of the artery due to one pulse beat has not relaxed before the next pulse beat comes along, thus giving virtually continued vaso-constriction and therefore " white " anger.

I can, and I am sure many of my readers will be able to, think of many other everyday conditions, such as shock and in the precipitation of coronary thrombosis, where such a mechanism of circulation would make more sense of the observed facts than Harvey's theory by itself.

Perhaps there was more in Leonardo's theory of the heart's function than present-day physiologists will allow.

Workington,
Cumberland. R. N. R. GRANT.

ANABOLIC STEROIDS IN URÆMIA

SIR,—We should like to comment on the preliminary communications by Dr. McCracken and Dr. Parsons, and Dr. Gjorup and Dr. Thaysen, in your issue of Oct. 25. We have been engaged for more than two years in animal experiments and clinical investigations into the influence of anabolic drugs on uræmia. In our animal experiments we used methandriol (' Sterediol ', ' Neosteron ', methylandrostendiol) and nandrolone ('Durabolin '), and their combination with methylthiouracil.

Male rats of the same weight were divided into eight groups, each group containing 10 animals. Each group received one of the following drugs or their combinations for five days: 5 mg. per day of methandriol, 125 mg. per day of methylthiouracil (' Basethyrin '); or 1·5 mg. per day of nandrolone, on 4 occasions. Thereafter the animals were subjected to bilateral nephrectomy under ether anæsthesia, and the drug was continued. The control group of 10 animals received no drug but was nephrectomised. The average survival-time of the controls was 78 hours. The survival time of the animals given methandriol was 18 hours (23%) longer; in the nandrolone group it was 4·6 hours (5·9%) longer, and in the methylthiouracil-treated animals 18·6 hours (24%) longer. With a combination of methandriol and methylthiouracil, the survival time was 13·2 hours (16·7%) longer; the nandrolone-methylthiouracil group lived on the average 19·3 hours (24·8%) longer than the controls, and the methandriol-nandrolone group 16·6 hours (21·3%) longer. Animals given all three drugs had a survival-time of 11 hours (14·2%) longer than the controls.

The non-protein-nitrogen (N.P.N.) values in the treated animals were at first somewhat lower than the controls, but at the end of the experiment they exceeded the control values because the treated animals were living longer.

Methandriol and nandrolone were used for the clinical investigations. These drugs were given to 50 unselected patients in the urological clinic with renal deficiency of different kinds.

Methandriol was given as tablets (25 mg. daily) or by intramuscular injection as crystalline emulsion. Nandrolone was given once or twice a week as 25 mg. intramuscular injections. Laboratory examinations followed the N.P.N. values, the alkali reserve, the total serum-protein, and the A/G ratio. In several cases paper electrophoresis was used. The fluid uptake, excretion, and body-weight were recorded. Among the subjective symptoms we noted the presence or absence of thirst or somnolence, and the appetite and the general state of the patient.

Of the 50 uræmic patients 38 had complex treatment, so that the evaluation of the course of their disease and the effect of anabolic drugs cannot be considered as exact.

14. Wagner, B. M. *in* Analytical Pathology (edited by R. C. Mellors). New York, 1957.

Of the 50 patients renal function was severely and irreversibly damaged in 12, who had no treatment except these two drugs. The causes of their disease were: solitary renal calculus (2 cases), solitary renal hydronephrosis (1), bilateral calculus with pyelonephritis (1), bilateral renal tuberculosis (4), bilateral chronic pyelonephritis (3).

Our observations in these 12 cases may be summarised as follows:

(1) The N.P.N. level slightly but regularly decreased in each case during administration of the drugs. The N.P.N. level also decreased when, during treatment, the patient was allowed more liberty in the low-protein diet.

(2) One or two weeks after stopping the drugs the N.P.N. levels began to rise and exceeded their initial value. They fell again after repeated administration of the drug.

(3) As a response to the drug, fatigability and thirst decreased, appetite improved, and sometimes the weight increased.

(4) The values of total protein and A/G, as well as the records of paper electrophoresis, were labile during and after treatment without showing characteristic changes.

The improvement and convalescence of patients receiving methandrine and nandrolone as well as other treatment was quicker and more favourable than in patients treated without the anabolic drugs.

These results were presented at the congress of the Hungarian Urological Society, Pécs, Sept. 11, 1958. They are also to appear in *Zeitschrift für Urologie* and *Magyar Sebészet*.

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Z. SZENDRÖI
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SEX REVERSAL

SIR,—Clinical medicine has its own scientific methodology and its own scientific standards, which are often different from those of pathology. Thus for the pathologist the nuclear sex-chromatin findings represent an absolute value, but for the clinician only a relative value. We cannot base ourselves for the determination of the sex—meaning the predominant, the pragmatic, sex—of an intersexual individual only on the sexual chromatin, but we have to take into consideration the total psychophysical personality of this individual, the balance of all sexual characters. The nuclear chromatin is one of these sexual characters; and the clinician, exercising his critical, synthetic, and individualistic-existential method, will assess its place in the whole picture.

The papers of Dr. Keith Moore and of Dr. A. Ferguson Smith in your issue of Jan. 31 seem to confirm this view, as they describe female sexual chromatin in individuals living completely as males, a few of them even normal, married, potent, and with possibility of male fertility. Are we going to force these individuals into the female sex on account of their positive sexual chromatin? Are we going to allow a child with hypospadic penis, scrotum without testes, and female nuclear sex in a girls' school? Are we to deny to transexualists (the most tragic of all intersexes) the benefit of a change of registration which would not do any harm to anyone and would prevent for those unfortunates a life of misery and even suicide, on the basis of their nuclear chromatin?

Our legislation regarding intersexual conditions is already very deficient, and the dogma of sexual chromatin will lead to even more erroneous legal decisions. For the clinician who will guide such legal decisions, the sexual chromatin is a part; and we cannot know the whole by considering only a part. Sex is a matter of total personality —including the most important, psychological personality —and not a matter of genes, gonads, genital organs, or endocrines.

London, W.1. A. P. CAWADIAS.

TUBERCULOSIS AMONG THE GURKHAS

SIR,—It was never my intention,[1] and I am sure that it was not yours,[2] to convey the impression that facilities for thoracoplasty were not available to the Gurkhas before 1957.[3]

To me the emphasis has always been on partial lung resection in respect of all irreversible pulmonary tuberculous disease of such an extent that it can be excised [4] and when the necessary facilities are available. To date there have been 96 major thoracic surgical operations on cases of tuberculosis in Gurkhas at the Army Chest Centre—namely, 92 partial lung resections (89 Gurkhas, 3 of whom had bilateral resections) and 4 thoracoplasties (3 Gurkhas, 1 of whom had bilateral thoracoplasty). A patient with bronchiectasis also had a resection. We have had no fatal cases, and no patient's postoperative up-grading has been delayed more than three weeks because of complications, all of which have been mild.

134 cases of tuberculosis in Gurkhas have been accepted provisionally for thoracic surgery out of 142 referred for opinion to the Army Chest Centre since March, 1957. To the Gurkha the operation of resection raised all sorts of doubt in his mind. How could he, a soldier man and boy, stand straight or march straight if a piece was cut out of one lung and a piece of the other lung not cut out to balance? That was one of the many questions posed.

Our aim in the treatment of pulmonary tuberculosis is to return the Gurkha to his former high degree of physical fitness so that, should he so desire, he may return to his beloved regiment and soldier on or return to a full and productive life in Nepal. In my opinion that aim is normally achieved by partial lung resection but not by thoracoplasty. The time available to me at the NAPT Commonwealth Chest Conference was of necessity limited, and so no reference to thoracoplasty by me will be understood.

Connaught Hospital (Army Chest Centre), Hindhead, Surrey. JOHN MACKAY-DICK.

VOMITING OF EARLY PREGNANCY

SIR,—I was interested in Dr. Coppen's study of genetically determined masculine deviations in the androgyny scores and of psychological factors in a group of primiparæ with early vomiting of pregnancy compared to a group of controls (Jan. 24).

I am sure, however, that Dr. Coppen will not claim more than a very minor role for hereditary factors in the ætiology of pregnancy sickness, in view of the great variation which ranges from absence of sickness to hyperemesis so often found in a series of pregnancies in the same woman. This variation, inexplicable in terms of physical factors such as climate, diet, or infection, forces on us consideration of other elements in the life situation.

My 1946 paper [5] to which he refers was initiated by the conviction that there was some kind of tie-up between "biliousness" in women (a disorder rarely found in males apart from acidosis in childhood) and deep sexual conflict. I had been impressed with the finding that non-pregnant parous women with a tendency to nausea and vomiting were not only sexually frigid as a class but had a history of more

1. Mackay-Dick, J. N.A.P.T. Commonwealth Chest Conference, London, 1958.
2. *Lancet*, 1958, ii, 1053.
3. Fairburn, A. *ibid.* Feb. 7, 1959, p. 310.
4. Mackay-Dick, J. *ibid.* 1958, ii, 422. Mackay-Dick, J., Slattery, D. A. D. *Brit. med. J.* 1958, i, 88.
5. *Lancet*, 1946, i, 336.

than average nausea and/or vomiting in their pregnancies. I had also met up with a few women who had had hyperemesis in their pregnancies to one husband, but had no nausea or vomiting in later pregnancies after marriage to a second husband. Here there was always frigidity to the first husband and sexual satisfaction with the second.

During the early 1940s I worked out the conceptions of: (1) disturbed sexual functioning (the repetition of undesired coitus); (2) mother attachment (the girl who, having first identified herself with her mother, later gave her all her love, often because she saw her having an unpleasant life with a drunken husband); and (3) previous dyspepsia (the girl who had grown to believe in sex as evil on account of the over-enthusiasm of her parents in their urge to prevent her being promiscuous in adolescence). These three factors, each bearing an antisexual significance at a different phase of life, seemed to me to contain the idea I wished to put to the test, as is shown in my paper.

To consider a physical disorder from a psychological viewpoint and at the same time attack the orthodox psychologists carries an inevitable penalty. I had to wait eight years before Harvey and Sherfry [2] confirmed my findings and another four years for Coppen to demonstrate a weakness in psychological methodology.

Glasgow. G. GLADSTONE ROBERTSON.

LOCAL REACTIONS TO POLIOMYELITIS VACCINE

SIR,—The poliomyelitis vaccine in common use contains small quantities of penicillin, probably less than 0·5 units per ml., an amount which is considered too small to produce sensitisation when given to a child.[3] It is possible, however, that even such small amounts of penicillin may produce reactions in persons who are already sensitised to penicillin. Vickers [4] has shown that very small amounts of penicillin in milk can produce severe skin reactions, and there have been reports of general and cutaneous reactions after poliomyelitis vaccination which appeared to have been due to the penicillin in the preparation.[5]

I report here 3 cases in which a local reaction appeared at the site of injection of poliomyelitis vaccine.

CASE 1.—In a boy of 14, twenty-four hours after injection of 1 ml. of poliomyelitis vaccine into the left upper arm, the skin around the site of the injection began to itch intensely. Next morning an area of erythema developed around the site of injection, and scattered over this area were a few small vesicles. More vesicles appeared during the next forty-eight hours, and four days after the injection the skin on the outer aspect of the left upper arm was red and covered with numerous vesicles of varying size and shape (see figure).

Skin reaction four days after poliomyelitis vaccination. Most of the vesicles are still intact but a few have been ruptured by scratching.

This boy had had osteomyelitis when he was 10, and had been given a long course of penicillin, but had never shown any untoward reaction to this antibiotic. Strangely enough he did show some reaction to cetrimide solution; and as this was used to clean his arm before the injection it is possible that this would have aggravated any reaction that may have been caused by the penicillin.

CASE 2.—A man of 48, an ambulance driver, was included in one of the priority groups for vaccination. At the time of the second injection, three weeks after the first, there was an area of desquamation on the outer surface of his left upper arm. He said that a few days after the injection the skin on his left upper arm became red, and several vesicles had appeared around the injection site. Two years previously he had used penicillin ointment to treat some spots on his chin, and his whole face had "blown up". At that time his doctor had warned him never to allow anyone to give him penicillin again.

CASE 3.—In a woman of 26, a nurse, an area of erythema developed around the site between one and two days after vaccination. It was accompanied by intense itching, but no vesicles developed. She had suffered so much from penicillin reactions in the past that she had been advised to abandon hospital nursing.

It is most likely that these local reactions were produced, in previously sensitised persons, by the penicillin in the vaccine preparation, and some years ago while investigating the history of a young man who died from penicillin anaphylaxis I discovered that a similar type of rash had developed at the site of the penultimate penicillin injection.

Although it has been suggested [6] that in a small proportion of deaths following poliomyelitis vaccination anaphylaxis seemed a definite cause, it is most unlikely that the small amount of penicillin in the poliomyelitis vaccine preparation would produce a fatal or even severe reaction. Nevertheless it may well produce a mild reaction of the type I have described and thereby reveal or confirm the presence of hypersensitivity to penicillin. The extension of poliomyelitis vaccination to the older age-groups may increase the number of such reactions; and it would be well to be on the lookout for them and inform the patient's own doctor, where necessary, since this may save some unsuspecting patient from a severe or even fatal reaction to penicillin.

I should like to thank Dr. J. Fielding, county medical officer of health, Holland, Lincs, for permission to publish these cases and Dr. G. Hird for providing details of case 3.

Public Health Department, Holland, Lincs. H. P. BURROWES.

DEATH OF A TESTICLE

SIR,—More words have been expended on the ascent and descent of the testicle than on the rise and fall of the Roman Empire. Would you, Sir, allow me a few paragraphs on the untimely demise of an organ which plays so notable a part in the human story?

Torsion of the testis is followed by gangrene of the organ in 80% of cases. This statement, taken from a standard work on surgery, is interesting because it is unexpectedly but manifestly false. Torsion is *never* followed by gangrene: a testicle so afflicted becomes a sterile infarct. The distinction is of some importance, because the body will contain a sterile infarct, but will try to discard any part which is both mortified and septic.

An infarcted testicle will stay in the scrotum, albeit a shadow of its former self, but the event is immediately followed by symptoms and signs which are almost identical with those of infective epididymo-orchitis—except that in the latter the temperature is higher, and abscess formation is relatively common.

2. Harvey, W., Sherfry, M. J. *Psychosom. Med.* 1954, **16**, 1.
3. Perry, W. L. M. *Brit. med. J.* 1956, i, 566.
4. Vickers, H. R., Bagratuni, L., Alexander, S. *Lancet*, 1958, i, 351.
5. *Brit. med. J.* 1958, ii, 843.
6. Payne, A. *Lancet*, 1958, ii, 796.

Certain practical conclusions may be drawn from the basic premise of a distinction between gangrene and infarction.

(1) It is not always essential to operate on cases of torsion. For example, a puny premature infant developed "orchitis" within 12 hours of birth, and was seen 2 days later. The diagnosis was clearly torsion, the prospects of testicular salvage were nil, and the risks of operative treatment were appreciable. Expectant treatment was rewarded by speedy resolution of the local signs, and commemorated by final atrophy.

(2) The diagnosis of torsion should be considered in all cases of mild "orchitis". A 15-year-old boy presented with a subsiding attack of "orchitis" associated with a small hydrocœle. 3 weeks later the testicle was explored, and the testis was found attached to the epididymis by a mesorchium which had twisted through half a turn. It was easy to fix the testis in a more stable fashion. This diagnosis is always considered in boys, but for some curious reason their elders seem to be regarded as immune.

(3) It is well known that hernial repairs in old men can be made more secure by dividing the spermatic cord, thus preserving both the patient's testicle and his illusions. This little subterfuge is, of course, followed by "orchitis"—and then by atrophy.

(4) The non-specific epididymo-orchitis which was so common among Servicemen in World War II has never been satisfactorily explained. Its dramatic onset, together with the absence of urinary infection and of suppuration, make one wonder whether it was merely a reflection of the outrageous physical exertions which were fashionable at the time, and in which the cremaster involuntarily participated.

Barnet, Herts. V. J. DOWNIE.

COLLODION THIMBLES FOR INJURED FINGERS

SIR,—The use of collodion reinforced thimbles and dressings for the protection of damaged digits is well known. The technique we employ is to form a two-layer tube gauze cover with or without underlying dressing and soak it with collodion stored in a polyethylene bottle.

The screw cap of the bottle has a hole pierced in an obliquely set plain surface—as in glue bottles. The plain surface rests on the dressing and helps to spread the collodion, the rate of flow of which is controlled by pressure on the pliable bottle. Excess of collodion, which forms a mass around the cap, is easily stripped free when it has dried.

General Hospital, Ashton-under-Lyne. A. WILKINSON.

THE GASTRO-AURICULAR PHENOMENON

SIR,—Malherbe [1] described 3 cases of œsophageal hiatus hernia associated with painful itching in the external meatus of the ear. He explained this as a referred pain along the vagus, irritation of the œsophageal filaments being misinterpreted centrally as coming from the auricular branch. In 2 of Malherbe's cases the diaphragmatic hernia was repaired and the itching disappeared; in the 3rd case, however, the itching disappeared without operation when the patient took a reducing diet with frequent small meals.

In 1922 I described [2] my "gastro-auricular phenomenon" which, I think, is either identical or closely related to Malherbe's phenomenon. Whenever I suffered from heartburn I also had intense itching in my left external auditory meatus. Bicarbonate of soda by mouth relieved the itching immediately. Sometimes it preceded the heartburn; and the more intense the one, the worse the other.

For some reason the itching disappeared after over 20 years, though the heartburn persisted. After reading Malherbe's article, I had an X-ray examination of my stomach by Dr. Ernest To, of Hong Kong, and a hiatus hernia was excluded.

The gastro-auricular phenomenon is quite common: I found 3 cases simultaneously in one surgical ward, and I was told by several doctors that they had the same symptoms.

My explanation of the phenomenon was similar to Malherbe's.

The cells of origin of the vagus are in the medulla oblongata, above the olive. Some of the cells form the dorsal nucleus visceralis, others form the medial nucleus ambiguus (motor). The fasciculus solitarius (sensory) is connected with the ganglion jugulare and ganglion nodosum. The auricular branch of the vagus, which is its only peripheral branch, emerges between these two ganglia. The trophic centre of the auricular branch is in the ganglion nodosum.

The left vagus in its lower course supplies, with its left branch, the fornix and the two upper thirds of the body of the stomach, its middle branch innervates the prepyloric part, and its right branch the liver. Of the right vagus, the left branch innervates the cardia, the small curvature, and a part of the body; its right branch spreads into the semilunar ganglion; and its middle branch innervates the posterior part of the prepyloric section. The two vagi are usually separate and seldom anastomose. These anatomical conditions explain why in most of my cases the itching was unilateral, and usually on the left.

The sensory endings in the stomach are stimulated under certain conditions—e.g., hyperacidity. The stimulus is passed to the ganglion nodosum where the ganglion cells of the auricular branch are also involved and react as if the stimulus came from the auditory meatus. The stimulus is passed through the fasciculus solitarius to the cortex.

An interesting observation of Professor Kuemmel, of Heidelberg University, suggests that the cortical sensory centre of the auricular branch is well circumscribed. He observed a patient who, in his epileptic aura, constantly felt a bilateral itching of the external auditory meatus, similar to the sensation described by my patients. In Kuemmel's patient, however, the stimulation was central.

I have found no mention of the gastro-auricular phenomenon in the literature. Some textbooks of otology mention "pruritus nervosus" of the external meatus in which the skin is normal. The cause is unknown, and at least some of these cases may represent the gastro-auricular phenomenon. Deutsch [3] described an "auricular phenomenon" consisting of hyperæsthesia in the sensory area of the auricular branch of the vagus in pulmonary tuberculosis. The hyperæsthesia was on the more affected side. This is a syndrome analogous to the gastro-auricular phenomenon, but the primary stimulation is in the lungs.

I referred [2] also to the analogy of the gastro-auricular phenomenon and Head's hyperalgesic zones.[4] Head noted that hyperalgesia of certain trunk zones is associated with circumscribed hyperalgesic zones of the head. He explained this phenomenon on the basis of transmission of visceral vagus stimulation to the trigeminal area.

The sensation of heartburn is generally believed to arise from regurgitation of acid gastric juice into the lower œsophagus. Such regurgitation is certainly facilitated by a lax cardia or a diaphragmatic hernia. It is, therefore, possible that the stimuli in Malherbe's cases were not the result of stretching, pressure, or inflammatory involvement of the vagus, but of regurgitation of gastric juice into the lower œsophagus.

Malherbe's third case supports such a mechanism: no operation was performed on the hernia, and after dieting and small meals the ear itching disappeared. It is very unlikely

1. Malherbe, W. D. F. *Lancet*, 1958, i, 1368.
2. Engel, D. *Med. Klin.* 1922, **18**, 1479.
3. Deutsch, M. *ibid.* 1919, **15**, 1090.
4. Head, H. *Brain*, 1893, part III, p. 1; *ibid.* 1894, p. 339.

that diet could change stretching of the vagus or inflammation, but hyperacidity in the lower œsophagus may have been reduced. In the two operated cases improvement may also have been due to prevention of regurgitation.

If neutralisation of the gastric juice with alkali suppresses the itching in the hernia cases, then the mechanisms are identical, and the term gastro-auricular phenomenon could be adopted for both. Should the hiatus hernia cases not react promptly to neutralisation, however, then Malherbe's explanation may be correct, and there are two closely related but not identical phenomena.

Hong Kong. D. ENGEL.

Obituary

JOHN NISSEN DEACON

M.C., M.B. Lond.

Dr. J. N. Deacon, formerly medical director and surgeon to the ear, nose, and throat department of Edgware General Hospital, died on Jan. 31 at the age of 66.

He was born at Selhurst, the son of Dr. J. G. Deacon, and he was educated at Epsom College. After qualifying from the London Hospital in 1915 he served with the R.A.M.C. in France, Italy, and Egypt, and was awarded the M.C. for his work. After he returned to civilian life he held clinical assistantships at the London Hospital and spent some years in practice in Tangier, where he was aural surgeon to the Benchimol Hospital. After his return to this country in 1927 he took up his appointment at Redhill Hospital (as Edgware General Hospital was then called). He saw it grow from a country hospital of 100 beds with a staff of 3 doctors under a board of guardians to a regional hospital with 710 beds, a large outpatient department, and a medical staff of 67.

Deacon was a born planner with a great eye for exact detail, a wide knowledge of hospital requirements, and a strong practical sense which made him relish the work of expansion. His methods attracted visitors from all parts of the world, and his ideas for hospital buildings were used in many areas outside Middlesex. Later his knowledge was of value to the committee on standardisation of hospital equipment, on which he served as chairman for some years. Although most of his time was necessarily spent on administration he continued to practise his specialty. He was a deft and careful surgeon, and the niceties of E.N.T. work gave scope for his talents for neatness and attention to detail. He devised many items of hospital equipment—the Redhill anæsthetic trolley, the ward blackboard and chalk beside each telephone, an operating-stool. Heraldry and genealogy were two of his interests, and he devised the badge for the Hendon Group of Hospitals.

G. H. J. writes:

"I arrived at Edgware in 1938, the time of the hospital's largest growth, and I remember Deacon dashing hither and thither with his tape-measure, ascertaining that shelves were placed at the right height, that trolleys would pass comfortably into and out of corridors, and that his staff got the apparatus they needed. At first he gave an impression of restless efficiency, a tendency to brusque impatience, and complete self-confidence. This impression was only partially correct, for he was inclined to moods of self-doubt and uncertainty and the brusque manner was his defence while he evaluated his man. Once he laid it aside, he would be a charming companion, for he had a very wide interest in human activity, both past and present, and could converse with wit and pungency on many subjects. He had great love of Italy and of its music and its painting, and his interest in the past was reflected in his membership of the Society of Genealogists. At least one remote parish owes the restoration and re-binding of its registers to his enthusiasm.

Dr. Deacon retired in 1957 because of ill health. He leaves a son and a daughter.

RALPH SESSIONS HODGE

M.R.C.S., D.P.M.

Dr. Sessions Hodge, director of the neuropsychiatric department of Musgrove Park Hospital, Taunton, died at Bridgwater on Jan. 31.

After qualifying from University College Hospital he joined his stepfather, the late Dr. E. R. Thompson, in general practice at Crewkerne. He became interested in psychiatry and was a clinical assistant at the West End Hospital for Nervous Diseases, London, travelling there twice a week.

As his experience in psychiatry grew he concerned himself particularly with child guidance, and helped in the development of this service in Somerset. When the Burden Neurological Research Unit opened at Bristol he became connected with it. As electroencephalography developed there he became interested in this, and in 1946 organised his own department in Taunton; and he was one of the earlier members of the Electroencephalographic Society. He was intensely interested in neurophysiology and endocrinology, and was an authority on epilepsy and delinquency. He was clinical psychiatrist to the Kingswood Classifying School under the Home Office, and a member of the International Criminological Society.

Despite increased work he maintained his other interests. He was divisional chairman of the British Medical Association in 1947 and president of the branch in 1954. He took a leading part in forming the West Somerset Medical Club. He also engaged in the cultural activities of the locality, becoming a member of the Amateur Dramatic Society, an officer of the Taunton Deane Arts Club, and president of the Taunton Book Club. At school and in hospital he was keen on hockey and tennis, and later he hunted with the Seavington hunt, of which he was joint secretary, the Taunton Vale foxhounds, and Taunton harriers. He was an able polo player, bred sheepdogs, and was a judge at their trials.

K. C. B. writes:

"No-one could have been long in the company of Ralph Sessions Hodge without appreciating his buoyant personality, his ready wit, and his genial companionship. He possessed boundless energy and his interests were wide, and there was seldom a meeting of the many societies of which he was a member, and to which he often contributed, which he did not make time to attend. His medical colleagues valued his opinion; and his reports, with their permissive recommendations, were a model of sound clinical judgment and literary skill. His optimism and ready understanding drew many people to him. The West Country has lost one of its great characters—an able psychiatrist and physician."

E. M. C. adds:

"It was rather typical of Ralph Sessions Hodge that he wrote a personal letter apologising for absence, as recently as Nov. 19, facing quite clearly the fact that he would not get to London again. The combination of gaiety and vigour, and a delight in fox-hunting, with Quaker seriousness and almost over-conscientious concern for the welfare of his patients and colleagues, made up an unusual personality. His clinical interests too were widespread; and the field of electroencephalography, straight psychiatry, and the ordinary "run-of-the-mill" work of a regional child-guidance clinic, all came his way. He was an exceptionally hard worker, but at the same time devoted to his family life and all the home interests that that brought to him. He will be greatly missed."

Dr. Sessions Hodge is survived by his wife and by three sons.

JOHN COLIN GREGORY

M.R.C.S., D.Obst.

Colin Gregory, who died suddenly at the age of 55 at the height of his powers, was known to all the world as a tennis player, and to a privileged few as a doctor. The privileged few include his contemporaries at University College Hospital, and his many devoted patients at Hemel Hempstead.

Colin Gregory came to University College Hospital with a fine tradition behind him, and those of us who were privileged to see his father and mother at work in Beverley do not find it difficult to see how he learned his fine understanding of people, his quick appreciation of their joys and troubles, and his sympathy for them. These gifts, with a sturdy independence and an enormous zest for life in all its aspects, made up the Colin Gregory whom we knew and loved, and we rejoiced that he had been given the quickness of mind and body which made him the master of many games and the wisdom and balance which prevented him from being the slave of any. The temptation was certainly there because he might have played cricket for Yorkshire in his early twenties, and later on, when he began to take squash rackets seriously, there were very few who could beat him. At golf, which he never took very seriously, his handicap was in single figures, and his occasional appearances on the rugger field showed very considerable promise as a fly-half.

Colin never allowed his supremacy at games to take his mind away from doctoring. This was in his blood, and it is sufficient to say that in a changing world and a changing environment his standards as a doctor remained the same. His patients had only to trust him, and they were assured of the best that effort and ability could give.

It is too easy to indulge in reminiscences of hours and days spent with Colin Gregory. The close friendship which has been such a joy to me began at University College Hospital when he was a student, and developed when he became my house-surgeon in 1929. I can well remember at this time a modest request, after a long morning's operating, for leave to depart in time to eat a sandwich on the way to Wimbledon where he was due to play in the early afternoon. At this very early time Colin showed the wisdom which always kept him as a true amateur. His enjoyment of a game was always greater if it was shared by his friends, and although their inexpert efforts did not pass without comment they certainly never spoiled his pleasure.

A little later when Colin became the resident medical officer of the hospital he turned his attention to squash rackets, and by his example and leadership produced a very creditable side out of very moderate material. The great event of the year was the Yorkshire tour, a light-hearted event which took us to Colin's native county with a side which generally included Dick Sloley. These tours were memorable, and Colin continued to enjoy them in retrospect until I last saw him a very short time before his death.

Shooting was another of Colin's interests which developed largely during his period at University College Hospital when a few enthusiasts made nocturnal journeys to and from Norfolk in order to enjoy a day's shooting without interfering too much with the week's work. Shooting continued to give Colin a great deal of pleasure, and characteristically, although he was a good enough shot to be welcome where birds were plentiful, he was equally happy to enjoy what sport could be had among his friends on the doorstep of his practice.

Perhaps the best memories of all are the evenings after one of these very domestic occasions when Colin could be seen at home completely happy with his wife and family attending to his dog, cleaning his gun, and dealing at the same time with the claims of a very large practice. How all this was done by the chairman of the All England Club we never understood, but there is no one among Colin's friends who can doubt that fifty-five years of his life carried the effort and produced the fruit of seventy years of any other.

A. J. G.

Public Health

Fog in Scotland

AT the end of January and the beginning of February fog was widespread and dense over the Forth and Clyde valley.

Glasgow

Glasgow's experience of fog this winter has been unusual. While some fog is normally present on some five to six days each winter month, this winter there have been two periods of major fog prevalence. The first was on Nov. 30 and Dec. 1, when the fog and ensuing smog were the worst for at least twenty-five years. The air pollution rose rapidly to a density ten times the usual winter level, but within thirty-six hours the smog had disappeared completely and the air was clear again.

In the next eight weeks fog was present intermittently. From Jan. 31 to Feb. 3 visibility was down to 0–25 yards; the temperature did not rise above freezing-point and at times was as low as 16°F, and hoar frost fell like snow.

There was an increase by about 25% in deaths from degenerative heart-disease both in December and in January. The incidence of pneumonia was high, but deaths from this disease corresponded fairly closely to those in the corresponding weeks of 1957 and 1958. Deaths from bronchitis, however, trebled in the weeks ended Dec. 6 and 13, and were doubled in the week ended Dec. 20, compared with the corresponding weeks in the previous year. Deaths from bronchitis again increased in January, and in the week ended Feb. 7 were four times as numerous as in the corresponding week last year.

In the Scottish Western Hospital Region only 75 more patients with bronchial disorders were admitted to hospital in the two weeks ended Jan. 31 than in the corresponding two weeks last year; but the illness was more severe than usual, and the mortality-rate in this group of patients was about three times greater than last year. Hospital staffs were themselves depleted through illness by about 20%.

Edinburgh

In Edinburgh fog was severe on Feb. 1 and Feb. 3. On Feb. 1 a "smog" warning was issued: elderly people and those with chest disorders were advised to remain indoors. There was no notable increase in mortality and morbidity.

We are grateful for information provided by Dr. W. A. Horne, medical officer of health for Glasgow; Dr. A. K. Bowman, senior administrative medical officer, Scottish Western Regional Hospital Board; and Dr. J. L. Gilloran, depute medical officer of health for Edinburgh.

London in 1957

IN a comprehensive report on the year 1957 [1] Dr. J. A. Scott, the county medical officer of health, discusses, among many other things, atmospheric pollution and immunisation.

Atmospheric Pollution

Dr. Scott remarks that examination of four fogs in the winters of 1954–55, 1955–56, and 1956–57 showed that a critical level of atmospheric pollution in relation to the effect on health was reached when mean daily concentrations were about 200 mg. of black suspended matter per 100 c.m. of air, and 40 parts of sulphur dioxide per 100 million parts of air. The fog of Dec. 2–6, 1957, reached this critical level; and, after analysing the mortality figures, Dr. Scott is satisfied that this fog accounted for 300 excess deaths—or 400 if the deaths resulting from the Lewisham rail disaster are included.

Immunisation

Smallpox.—In the years from 1949 to 1957 the numbers of children under 1 year of age who were vaccinated, expressed

1. London County Council: report of the county medical officer of health and principal school medical officer for the year 1957. Published by the Council, County Hall, Westminster Bridge, S.E.1. Pp. 205. 2s. 6d.

as percentages of live births in each year, were as follows: 25, 31, 38, 45, 48, 49, 50, 49, 56. "The present level of infant vaccination is substantially higher than the level achieved during the later years of the Vaccination Acts, a fact which vindicates the expectations of those responsible for repealing the Acts."

Diphtheria.—Only 4 cases of diphtheria were notified in 1957. The percentage of children immunised at 5 years of age fell from 67·0 in 1950 to 63·0 in 1952, but subsequently rose to 70·4 in 1957. Nevertheless, this proportion is "far from satisfactory".

"The main factors against the attainment of high levels of immunisation have been apathy, organised hostility, exaggerated fear on the part of parents of the possibility of poliomyelitis following inoculation and measures taken by divisional medical officers to reduce the amount of immunisation during local prevalence of poliomyelitis."

There can be little doubt, says Dr. Scott, that a factor which has helped to maintain higher levels of diphtheria immunisation has been the possibility of combining this with vaccination against whooping-cough.

Whooping-cough.—In 1957 nearly 90% of the whooping-cough immunisation was carried out in the form of combined diphtheria/whooping-cough prophylactic, with or without tetanus toxoid. The number of primary inoculations, expressed as a percentage of live births, was 66·8.

"While there is abundant evidence of the value of the vaccine to the individual child in reducing the likelihood of infection and in reducing the severity of the attack when complete protection is not conferred, the precise part played by vaccination in the recent favourable community experience cannot be clearly shown. In view of the demonstrable benefit to the individual it is reasonable to believe that the use of the vaccine has assisted in the production of the comparatively low figures of mortality in recent years. It is doubtful if a substantial reduction in incidence can be expected unless further attention is given to the problem of maintaining immunity by reinforcing doses. In so far as this could be done by combined diphtheria/whooping cough prophylactics, in those whose primary course was of this nature, no problem would be presented. However, as whooping cough, unlike diphtheria, is a comparatively mild disease in older children many people feel that it would not be justifiable to embark on organising repeated booster doses of whooping cough vaccine."

Tetanus.—In January, 1957, the Ministry of Health approved a scheme submitted by the L.C.C. for immunising children under 5 years of age against tetanus, using the triple prophylactic. During the year over 12,000 children were immunised in this way, nearly 30% of them by general practitioners.

Infectious Diseases in England and Wales

Disease	Week ended January				
	3	10	17	24	31*
Diphtheria	4	5	5	4	1
Dysentery	886	675	839	1194	1081
Encephalitis:					
Infective	3	3	3	1	2
Post-infectious	...	1	2	4	5
Food-poisoning	154	148	107	200	157
Measles, excluding rubella	18,180	15,140	12,675	13,710	18,025
Meningococcal infection	25	25	24	40	31
Ophthalmia neonatorum	26	27	17	19	19
Paratyphoid fever	2	9	37	43	8
Pneumonia, primary or influenzal	722	550	527	611	679
Poliomyelitis:					
Paralytic	23	26	21	14	20
Non-paralytic	8	17	5	4	1
Puerperal pyrexia	204	210	172	253	199
Scarlet fever	1151	777	1103	1428	1396
Smallpox	..	..	..	..	..
Tuberculosis:					
Respiratory	486	467	481	476	528
Meninges and C.N.S.	5	7	6	6	2
Other	42	45	42	61	54
Typhoid fever	1	1	1	1	15
Whooping-cough	584	530	508	658	859

* Not including late returns.

Notes and News

W.H.O. EXECUTIVE BOARD

THE Executive Board of the World Health Organisation, which met in Geneva from Jan. 20 to Feb. 3,[1] recommended a working budget of $16,418,700 for W.H.O. in 1960. This represents an increase of $1,251,960 (8·25%) over the corresponding estimate for 1959. The Board also recommended adoption of the programme of work for 1960 submitted by Dr. M. G. Candau, the director-general. This programme calls for increased activity with regard to malaria, tuberculosis, endemoepidemic diseases, public-health administration, nursing, social and occupational health, health education of the public, nutrition, and education and training of health personnel. These recommendations will be placed before the World Health Assembly, which opens in Geneva on May 12.

The Board studied a resolution by the General Assembly of the United Nations inviting W.H.O. to consider organising an International Health and Medical Research Year, with the aim of intensifying international cooperation against major killing and crippling diseases. The World Health Assembly will be called on to make a final decision.

CHILDREN IN THE CARE OF THE LOCAL AUTHORITIES

ON March 31, 1958, there were 62,070 children in England and Wales in the care of the local authorities.[2] Of these 27,337 (45%) were boarded out. The average weekly cost of keeping a boarded-out child was £1 17*s.* 8*d.*, compared with £7 14*s.* 3*d.* for a child in a local-authority home. The average weekly parental contribution per child was 5*s.* 3½*d.* Of the 40,000 children received into care during 1957–58, 24,000 came into care because of the infirmity or temporary illness of a parent or guardian. Almost 22,000 were under five years of age.

PHARMACOPŒIA FOR SICK CHILDREN

THE publication of a revised *Pharmacopœia of The Hospital for Sick Children, Great Ormond Street*,[3] is an event of some interest, for a revolution in therapeutics has taken place in the span of a quarter of a century since the last edition. One of the most welcome improvements in the care of children has been the replacement of nauseating draughts and potions by tablets and pleasant-tasting syrups. This advance has to some extent been offset by the greater number of specific remedies which must be given by injection, so that the child's horror of "medicine" has largely been transferred to "the needle". Happily, this undesirable trend is being reversed by the increasing introduction of preparations which are effective when given by mouth.

The new edition of the *Pharmacopœia* reflects the changing face of pædiatric therapy by including many new monographs on tablets and injections. Nevertheless, it is disappointing to find that a large part of the book still consists of complex prescriptions, some of which can only be regarded as of historical interest. A conservative approach to the work of revision, and reluctance to discard the time-honoured prescriptions of the past, are understandable; but it is difficult to believe that the *Pharmacopœia* really represents the day-to-day practice of a modern children's hospital. How often is mist. bromoform prescribed, and what therapeutic benefit is expected from 1 grain of potassium chlorate in 60 minims of water? It is satisfying to find that mist. ol. ricini has disappeared, but could not mist. aloe. co. have been omitted as well when so many more pleasant alternatives are available?

The most valuable part of this work is the appendix, which gives concise information about antibiotics, hormones, anticonvulsants, and other drugs, with details of the doses suitable for children. The up-to-date *National Formulary* greatly diminishes the need for individual hospital pharmacopœias;

1. See *Lancet*, Jan. 31, 1959, p. 263; *ibid.* Feb. 7, p. 320.
2. Cmnd. 632. H.M. Stationery Office. 1959. Pp. 9. 9*d.*
3. Copies are obtainable from the secretary of the hospital, Great Ormond Street, London, W.C.1. 10*s.* 6*d.*, plus 6*d.* postage.

out, if justification for the publication of this volume is required, it is to be found in the appendix, which might be expanded to form the main substance of future editions.

A WATERPROOF ADHESIVE EYESHIELD

A SHIELD for the eye during dermabrasion, designed by Dr. Napier Thorne, has proved its value in 18 months' use in the skin departments of the London Hospital and the Prince of Wales's General Hospital, Tottenham.

Dermabrasion, or skin planing, is frequently done for the facial scarring of acne vulgaris, and the refrigerant 'Arcton', used as local anæsthetic, could get into an unprotected eye.

The shield is applied as shown in the figure over a greased gauze pad placed on the closed eyelid. It is made of a waterproof pink non-stretchable polyvinyl-chloride plastic sheet; one surface is covered with a zinc-oxide adhesive and backed with muslin, which should be removed immediately before use.

These eyeshields, which might have many other uses, may be had (in boxes of 3 dozen) from Dalmas Ltd., Junior Street, Leicester. The photograph was taken by the photographic department of the London Hospital.

WORK TABLES

ASSURANCE companies have long found "life tables" useful in determining life-assurance premiums and annuity-rates. The Ministry of Labour and National Service have used this actuarial device in their booklet on the *Length of Working Life of Males in Great Britain*,[1] which gives figures showing a man's average expectation of working life. Like the life table, the tables of working life assess future probabilities on the basis of past experience; the figures can hold good only if conditions remain unchanged. Also, as the booklet points out, "retirement, unlike death, is not clear cut", and the degrees and uncertainties which surround it have increased the difficulty of calculating the tables. The information they offer will be valuable to those responsible for administering both private pension schemes and public social services, but it is a sobering thought for the rest of us that the 10,000 boys born alive in 1931 can expect to face 406,018 man-years at work.

TRAVELLER'S MEDICAL GUIDE

A NEW guide for the health-conscious American traveller [2] has sections on immunisation and the health problems of travel (including those of children), a glossary of diseases, advice on first-aid, and translations of medical complaints into French, Italian, and Spanish. The greater part of it, however, is a gazetteer of countries, giving brief descriptions of the chief tourist (and U.S.A.F.) centres, with notes on climate, purity of water, health hazards, main hospitals, medical associations and medical schools, and the type of medical care available and how to get it. So far so good; but unfortunately this mass of useful facts, elicited by correspondence with over three thousand persons, has not been edited by anyone with first-hand knowledge of the country—at any rate of Great Britain.

Thus for each of the 25 British centres mentioned, including the "Urban District of Lakes", the health department is solemnly recorded as not recommending bottled water. On the other hand, the instructions for obtaining a doctor vary widely. In Bath, Southampton, and Newport (Isle of Wight), the traveller should get in touch with the medical officer of health; in Ipswich and Swindon he should go to the local hospital; in Leicester and Winchester to the police; in York and Brighton to the executive council; in Blackpool to the municipal health centre; in Glasgow to the Red Cross; and in Liverpool to the consulate of the traveller's nationality. The health hazard of London is rightly given as the absence of central heating in museums and historical buildings; in Coventry vaccination against smallpox and poliomyelitis is advised; in Warrington smallpox, typhus (sic), and paratyphoid are health perils; while Stratford-on-Avon is apparently free from anything of the kind.

Still, to produce such a guide is difficult, and probably there is more need of it when travelling to places like Bogota, Dhahran, or Khorramshahr. It will be a comfort if "I am sick to my stomach", or "mi sgocciola il naso", to know that in either case "mi factor sanguineo Rh es positivo."

1. H.M. Stationery Office. 1959. Pp. 24. 3s. 6d.
2. The World Traveler's Medical Guide. By RICHARD T. ATKINS, M.D., and JANE MCGLENNON ATKINS. New York: Simon & Schuster. 1958. Pp. 399. $1·95.

University of Birmingham

Dr. A. L. Haigh has been appointed lecturer in physiology.

Royal College of Physicians of Edinburgh

At a meeting of the college held on Feb. 3, with Dr. A. Rae Gilchrist, the president, in the chair, the following were elected to the membership:

J. A. S. Hall, Sidney Sax, Chandawimala de Silva Mutucumarana, Harbans Kaur Virik, Sharad Gajanan Talpade, Vasant Krishnarao Tipnis, B. B. Beeson, M. C. J. Hunt, Thakur Baidyanath Prasad, J. F. Ryan, Mary R. Kerr, R. G. Mitchell, George Michell, Vinod Ratilal Mody, R. E. H. Partridge, R. D. Fine, G. K. Hargreaves, Saravanamuttu Satkurunathan, Susila Rajagopalan, A. N. Turnbull, Boris Fistein, Nabendu Kumar Sarker, Kenneth Davison, G. E. Gale, Philip Markman, Saiyid Abdul Wahid, Kwang Hoh Tan, Shapur Naimi, Kathleen M. MacWilliam, Kazi Abdul Azeem, Tikendra Raisinhji Desai, Dulal Chandra Brokotoky, W. W. Buchanan, F. E. Kenyon, G. J. Mackenzie, D. M. Pendreigh, James Syme, Cheng Hong Lim, Shaukat Raza Khan, W. E. S. Kiernan, Pinaki Bandyopadhyaya, R. G. Spector, Peter Leyburn, J. C. J. L. Bath.

Dr. S. H. Davies has been awarded the Kirk Duncanson fellowship, and Dr. Ferdinand Fok a Hill Pattison-Struthers bursary for 1959.

Harveian Society of London

The Buckston Browne prize for 1958, for an essay on the Clinical Significance of Tiredness, has been awarded to Dr. R. N. Tattersall.

International College of Surgeons

European meetings of this college will be held as follows: German section in Hamburg, June 1–3; French section in Lyons, June 19–21. The annual congress will be held in Chicago from Sept. 13 to 17. The biennial international congress will be held next year in Rome from May 15 to 18. Further particulars may be had from Dr. J. F. Brailsford, 20, Highfield Road, Edgbaston, Birmingham, 15.

Ergonomics' Place in Industry

The Ergonomics Research Society will hold a symposium on this subject at Oxford University from April 6 to 9. Further particulars may be had from Dr. S. Griew, Department of Psychology, 22, Berkeley Square, Bristol, 8.

Health in Middle Age

The Central Council for Health Education will hold a seminar on this subject, for medical officers of health at the Ivanhoe Hotel, Bloomsbury Street, London, W.C.1, from Feb. 24 to 27. Further particulars may be had from the medical director of the Council, Tavistock House, Tavistock Square, W.C.1.

At the annual meeting of the British Supporting Group for the World Medical Association held recently at B.M.A. House, Dr. T. H. Manners Kerfoot was elected president for 1959 in succession to Dr. Alexander Hall, former president of the British Medical Association. Dr. Kerfoot is also president of the Association of British Pharmaceutical Industry.

A course of six lectures on refraction work will be given by Dr. T. H. Whittington at the Royal Eye Hospital, St. George's Circus, London, S.E.1, on Thursdays from April 2 to May 7, at 5.30 P.M.

A series of lectures and lecture-demonstrations on manipulation is to be held at B.M.A. House, London, W.C.1, on Saturdays, April 4, May 2, June 6, and July 4, from 9.30 A.M. to 5.30 P.M. The fee for each day is 2 guineas. Particulars may be had from D. Alan Stoddard, 119, Harley Street, W.1.

A course on the chronic rheumatic diseases will be held at the rheumatism unit of St. Stephen's Hospital, Fulham Road, London, S.W.10, on Saturday and Sunday, March 14 and 15. Further particulars may be had from the secretary, Fellowship of Postgraduate Medicine, 60, Portland Place, W.1.

A course on fundamental and practical aspects of diabetes will be held by the University of Cambridge Postgraduate Medical School, at Addenbrooke's Hospital from April 16 to 18. The fee for the course is 5 guineas, and registration forms may be had from the secretary of the Medical School, Tennis Court Road, Cambridge.

Dr. M. M. Whittet has been appointed a member of the Scottish Advisory Council on the Treatment of Offenders.

A Challenge: Living a Full Life without Sight.—This Ministry of Health leaflet describes services which are ready to help newly blind people. These include home teachers and residential reablement centres. Copies of the leaflet have been sent to local authorities for distribution through their welfare service, and to hospitals with eye departments for the information of almoners.

A 16 mm. 'Kodachrome' optical track sound film, running for 25 minutes, has been made showing the facilities of the Slough Industrial Health Service, including Farnham Park Rehabilitation Centre, and of the occupational hygiene service. It can be borrowed free of charge, apart from postage, from the headquarters of the service, Community Centre, Farnham Road, Slough.

A British standard for electrically heated incubators and cots for babies (B.S. 3061 : 1958) has been issued by the British Standards Institution, 2, Park Street, London, W.1, from whose sales branch copies (6s.) may be obtained.

CORRIGENDA: *Mental Health Bill.*—In Dr. J. A. R. Bickford's letter last week the penultimate paragraph should have read: "The local authority also *approves* [not *appoints*] the psychiatrists who are signatories to recommendations for compulsory admission." In his second paragraph, the words *living conditions* should have been qualified by *in the broadest sense.*

Sydenham's Chorea.—The paper by N. W. Winkelman and J. L. Eckel cited in this annotation (Feb. 7, p. 297; footnote 6) was published in 1932.

Diary of the Week

FEB. 15 TO 21

Monday, 16th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.2
4 P.M. Sir Reginald Watson-Jones: Surgery is Destined to the Practice of Medicine. (Hunterian oration.)

UNIVERSITY COLLEGE, Gower Street, W.C.1
5 P.M. Prof. Alexander Haddow: The Chemistry and Biology of Cancer. (Second of three lectures.)

POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W.12
4 P.M. Dr. Brian Ackner: Emotional Aspects of the Menopause.

GUY'S HOSPITAL, S.E.1
5.15 P.M. Prof. C. E. Dent, Dr. M. Harrison: Hyperparathyroidism.

UNIVERSITY OF ST. ANDREWS
4 P.M. (Department of Medicine, Dundee.) Dr. J. M. Dodd, Mr. K. Ferguson: Methods of Assay of Thyroid Stimulating Hormone and its Applications.

Tuesday, 17th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P.M. Dr. W. A. H. Rushton: Visual Pigments in the Living Eye of Normal and Colour-blind Men. (Edridge-Green lecture.)

UNIVERSITY OF LONDON
5.30 P.M. (London Hospital Medical College, Turner Street, E.1.) Prof. E. Bueding (New Orleans): Mechanism of Action of Schistosomicidal Agents.

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Dr. Lynne Reid: Chronic Bronchitis and Hypersecretion of Mucus.

ST. MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W.2
5 P.M. Mr. E. M. Edwards: Genital Tuberculosis.

INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. R. G. Cochrane: Leprosy. (First of two lectures.)

UNIVERSITY OF LIVERPOOL
5.15 P.M. (New Medical School.) Mr. A. L. Eyre-Brook: Malignant Tumours of Bone.

UNIVERSITY OF ST. ANDREWS
5 P.M. (Physiology Department, Dundee.) Prof. Adam Patrick: Disseminated Sclerosis. (First of two lectures.)

Wednesday, 18th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5 P.M. *Comparative Medicine.* Dr. C. H. Andrewes, Miss G. Worthington, Dr. H. P. Chu: Respiratory Virus Infections of Man and Animals.
8.15 P.M. *General Practice.* Dr. W. H. Leake, Mr. R. F. Guymer, Dr. P. L. Bidstrup, Dr. R. J. F. H. Pinsent: The Contribution of the General Practitioner and the Industrial Medical Officer to the Health of the Community.

POSTGRADUATE MEDICAL SCHOOL
2 P.M. Dr. A. T. Sandison: Inflammatory Mastitis.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. J. T. Ingram: Psoriasis.

INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Mr. T. Holmes Sellors: Atrial Septal Defects.

UNIVERSITY OF ST. ANDREWS
4 P.M. (Department of Medicine, Dundee.) Dr. P. B. Marshall: Value of Catechol Amine Assays—Adrenaline and Noradrenaline Metabolism.

Thursday, 19th

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.1
5 P.M. Mr. P. J. Kerley: Mass Radiography in the Prevention of Disease—a Survey of 400,000 Boys aged 18.

ROYAL COLLEGE OF SURGEONS OF ENGLAND
3.45 P.M. Dr. A. Howe: The Neurohypophysis—a Review of its Structure and Function. (Arnott demonstration.)
5 P.M. Prof. Arnold Sorsby: Retinal Aplasia, Recessive and Dominant Forms.

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. R.H Mole: Radiation as a Toxic Agent.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, Manson House, 26, Portland Place, W.1
7.30 P.M. Prof. K. R. Hill: Aspects of Liver Disease in the West Indies.

BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, W.1
8 P.M. Dr. R. S. Pointon, Dr. J. J. Stevenson, Dr. J. K. Davidson: Radiographic Techniques Used in Treatment Planning.

MANCHESTER MEDICAL SOCIETY
8 P.M. (Staff House, University of Manchester.) *Anæsthetics.* Prof. W. D. M. Paton: The Effects of Halothane on Autonomic Nervous Activity.

LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant, Liverpool, 3
8 P.M. Dr. Keith Simpson: The Pathologist's Part in C.I.D. Investigations.

UNIVERSITY OF ST. ANDREWS
5 P.M. (Physiology Department, Dundee.) Dr. J. F. Goodwin: Pulmonary Hypertension.

Friday, 20th

ROYAL SOCIETY OF MEDICINE
5.30 P.M. *Epidemiology and Preventive Medicine.* Dr. W. P. D. Logan: Occupational Mortality.
8.15 P.M. *Radiology.* Dr. Jens Nielsen (Copenhagen), Sir Stanford Cade, Dr. Ralston Paterson, Mr. C. P. Wilson: The Changing Pattern of Oropharyngeal Cancer.

POSTGRADUATE MEDICAL SCHOOL
10 A.M. Mr. H. Osmond-Clarke: Cervical Disc Lesions.
4 P.M. Dr. S. W. Stanbury: Osteomalacia.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
3.30 P.M. Mr. C. Gill-Carey: Emergencies in Throat, Nose, and Ear Practice.

BRITISH TUBERCULOSIS ASSOCIATION
5 P.M. (26, Portland Place, W.1.) Mr. James Gow, Mr. Howard Hanley, Dr. Harwood Stevenson: Genito-Urinary Tuberculosis. (Members of the British Society of Genito-Urinary Surgeons will be welcome at the meeting.)

FACULTY OF RADIOLOGISTS
4 P.M. (Royal College of Surgeons.) Prof. A. Bradford Hill, Prof. Robert McWhirter, Dr. J. W. Boag: Statistical Problems Which Arise in Cancer Therapy.

ROYAL MEDICO-CHIRURGICAL SOCIETY OF GLASGOW, 242, St. Vincent Street, Glasgow, C.2
8.30 P.M. Dr. T. N. Fraser, Mr. Archibald Macdougall, Dr. J. M. Cameron: Management of the Painful Hip.

Saturday, 21st

LEEDS NEUROLOGICAL COLLOQUIUM
11 A.M. (General Infirmary, Leeds.) Sir Francis Walshe: What We Have to "Unlearn" about the Anatomy and Physiology of the Nervous System. (First guest lecture.)

Appointments

AMBROSE, ANNE, M.B. Lond.: registrar in psychiatry, Hellesdon Hospital, Norwich.

AUNGLE, P. G., M.B. Edin., M.R.C.P.E., D.P.M.: deputy physician superintendent, Dundee Royal Mental Hospital.

BALFE, R. J., M.B. Dubl.: senior casualty officer, Rotherham Hospital.

CREAMER, BRIAN, M.D. Lond., M.R.C.P.: consultant physician, St. Thomas' Hospital, London.

DOUGLAS, GWENTH J. E., M.B. St. And.: part-time S.H.M.O., mother-and-baby unit, Banstead Hospital, Surrey.

EVANS, K. T., M.B. Birm., M.R.C.P., F.F.R., D.M.R.D.: consultant radiologist, United Bristol Hospitals.

HENDRY, J. McI., M.B. Glasg.: assistant orthopædic and casualty surgeon, orthopædic department, Royal Alexandra Infirmary, Paisley.

JACKSON, A. D. M., M.D. Lond., M.R.C.P., D.C.H.: part-time consultant, children's department, London Hospital.

MCCAFFREY, MARGARET T., M.B. N.U.I., D.C.H., D.P.H.: deputy senior M.O., Manchester.

NICKOL, K. H., M.B. Lond., M.R.C.P.: senior registrar in chest medicine, Cambridge area chest clinic.

PHILLIPS, A. H., M.B. Lond., F.F.A. R.C.S.: consultant anæsthetist based at Royal Gwent Hospital, Newport, Mon.

REID, J. J. A., M.B. St. And., D.P.H.: deputy M.O.H. and deputy school M.O., Northamptonshire.

UDALL, G. S., M.B. Cantab., D.C.H., D.P.H.: senior assistant M.O., Brentford and Chiswick, Heston and Isleworth, and Southall.

WADE, COURTENAY C., M.B. St. And.: deputy group administrative medical superintendent, Dundee general hospitals.

Manchester Regional Hospital Board

DALBY, J. E., M.B. Cantab., D.M.R.T.: assistant radiotherapist (S.H.M.O.), Christie Hospital and Holt Radium Institute.

HARPER, T. A., M.B. Madras: assistant pathologist (S.H.M.O.), South Manchester group of hospitals.

STEWART, J. G., M.B. Aberd., F.F.R., D.M.R.T.: consultant radiotherapist, Christie Hospital and Holt Radium Institute.

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